

**PREOPERATIVE AND POSTOPERATIVE  
CARE OF SURGICAL PATIENTS**

# Preoperative and Postoperative Care of Surgical Patients

*By*

**HUGH C. ILGENFRIITZ, A.B., M.D., F.A.C.S.**

Formerly Assistant Professor of Surgery, Louisiana State University School  
of Medicine, and Visiting Surgeon, Charity Hospital  
of Louisiana at New Orleans

*with*

**FOREWORD BY**

**URBAN MAES, M.D., D.Sc., F.A.C.S.**

Emeritus Professor of Surgery, Louisiana State University School of Medicine;  
Consulting Surgeon, Charity Hospital of Louisiana at New Orleans,  
Consulting Surgeon, Touro Infirmary, Consulting Surgeon,  
Veterans Administration Hospital, New Orleans

**ILLUSTRATED**

St. Louis

**THE C. V. MOSBY COMPANY**

**1948**

COPYRIGHT, 1948, BY THE C. V. MOSBY COMPANY  
*(All rights reserved)*

Printed in the  
United States of America

*Press of*  
*The C. V. Mosby Company*  
*St. Louis*

## FOREWORD

Although the purely technical side of surgery has changed in many details in recent years, the advances in operative procedure have not kept pace with those resulting from the scientific investigations being made in the laboratory. The greatest recent progress in surgery is in the physiologic aspects of care of the patient before and after operation. By clinical application of investigative studies, it has become possible to perform more extensive operations and to attain an increased percentage of recoveries in procedures that would not have been attempted only a few years ago.

Much valuable information has been gained during the period of World War II. During this time, the use of whole blood, plasma, and the crystalline solutions has been put on a sound basis. The large-scale use of whole blood has been made safer by detailed studies in blood groups and subgroups, which will prevent some of the disagreeable and often serious effects which were formerly seen. Now that the Rh factor is better understood, fewer transfusion reactions can be expected. Fluid balance can be achieved on a much more accurate and scientific basis. Deficiency states, particularly those due to protein loss, and the consequences of such states can be treated with gratifying results. Further progress must be noted in chemotherapy. The use of the sulfonamides has been put on a more rational basis and the life-saving possibilities of penicillin and streptomycin have been explored to good effect. The laboratory is pursuing further studies along this line.

The recovery of patients after surgical operations is always the earnest wish of every surgeon. The successful handling of shock, hemorrhage, and infection is a primary consideration. While great advances have been made in the control of the first two, the conquering of infections is still a major problem. It is probable that future advances in surgery will continue to be made by earlier diagnosis, the correction of nutritional deficiencies and disturbed body chemistry, and the control of infections. It would seem, therefore, that the laboratory will give us the next advances that are to be made. The physiologist and the biochemist are the ones to whom we are looking.



sedative medication. Thanks are due also to Miss Catherine Hairston for her assistance in preparation of the manuscript, to Mr. W. B. Stewart for his cheerful cooperation in preparing the original illustrations, and especially to my wife for her constant encouragement and unselfish patience.

HUGH C. ILGENRITZ

Shreveport, Louisiana

# CONTENTS

	Page
CHAPTER 1. GENERAL AIDS	17
CHAPTER 2. FLUID AND ELECTROLYTE BALANCE.	21
Physiologic Regulation	21
Fluid Intake and Output	22
Acid-Base Balance	23
Indications for Replacement Therapy	27
Examination of the Blood	27
Examination of Urine	28
Principles of Corrective Treatment	29
Complications of Fluid Therapy	34
Administration of Fluids	35
Proctoclysis.	35
Hypodermoclysis	36
Intravenous Fluids.	38
Intraperitoneal Transfusion	43
Intramedullary Administration	44
CHAPTER 3. METABOLISM AND NUTRITION	50
Carbohydrate Metabolism	50
Carbohydrate Digestion	50
Carbohydrate Metabolism	51
Fat Metabolism	53
Fat Digestion	53
Fat Metabolism	55
Protein Metabolism.	58
Amino Acids	59
Protein Digestion	60
Protein Metabolism	61
Plasma Proteins	62
Protein Loss	64
Effects of Protein Deficiency	66
Protein Replacement	68
Acute Protein Deficiency	68
Chronic Protein Deficiency	68
Protein Substitutes	69
Oral Protein Replacement	70
Feedings by Tube	73
Corrective Dietary Therapy	78
CHAPTER 4. SEDATIVE MEDICATION	83
Hypnotic Drugs	83
Chloral Hydrate	83
Paraldehyde.	84
Barbiturates	84
Analgesic Drugs	87
Opium Alkaloids.	87
Preoperative Sedation	92
Choice of Anesthetic Agent	97
CHAPTER 5. GENERAL PREOPERATIVE MEASURES . . . . .	102
Permission. . . . .	103
Reassurance . . . . .	103
Examination	104
Metabolic Disorders.	106
Intercurrent Infections.	107

	Page
Specific Measures	108
Preoperative Medication	108
Elimination	108
Local Measures	109
Emergency Operations.	110
<b>CHAPTER 6. GENERAL POSTOPERATIVE MEASURES..</b>	<b>111</b>
In the Operating Room . . .	111
Recovery From Anesthesia . .	112
Position . . . . .	114
Maintenance of Body Heat. . .	117
Sedation. . . . .	118
Nausea . . . . .	120
Prevention of Complications	120
Fluid Balance	122
Diet . . . . .	124
Elimination . . . . .	126
Getting Up. . . . .	127
Encouragement. . . . .	131
<b>CHAPTER 7. SHOCK</b>	<b>132</b>
Pathogenesis . . . . .	133
Primary Shock . . . . .	133
Secondary Shock. . . . .	134
Postoperative Shock . . . . .	139
The "Crush Syndrome" . . . . .	140
Diagnosis . . . . .	141
Treatment . . . . .	143
Prophylaxis . . . . .	143
Therapy . . . . .	144
<b>CHAPTER 8. TRANSFUSION. . .</b>	<b>159</b>
Indications. . . . .	159
Hemorrhage. . . . .	159
Shock . . . . .	161
Preoperative and Postoperative Care . . . . .	162
Hemorrhagic States. . . . .	163
Contraindications . . . . .	164
Blood Grouping and Cross Matching	165
Rh Blood Type . . . . .	169
Methods of Blood Transfusion . . . . .	173
Collection of Blood . . . . .	175
Administration of Blood . . . . .	177
Transfusion Reactions. . . . .	181
Hemolytic Reactions . . . . .	181
Pyrogenic Reactions. . . . .	184
Allergic Reactions.. . . .	185
Blood Banks.. . . .	185
<b>CHAPTER 9. SYSTEMIC COMPLICATING FACTORS . . . . .</b>	<b>190</b>
Extremes of Age . . . . .	190
Infants and Young Children. . . . .	190
Aged . . . . .	197
Coincidental Infection. . . . .	202
Oral Sepsis. . . . .	202
Other Foci of Infection. . . . .	203
Early Syphilis. . . . .	203
Obesity. . . . .	203
Malnutrition. . . . .	203

	Page
Vitamin Deficiency States.	207
Vitamin A	207
Vitamin B Complex	208
Vitamin C	211
Vitamin D	211
Vitamin E	212
Vitamin K	212
Anemia	213
Acute Hemorrhage	213
Chronic Secondary Anemia	211
Hemolytic Jaundice	216
Sickle-Cell Anemia	217
Pernicious Anemia	217
Hemorrhagic Tendencies	218
Scurvy	218
Hemophilia	218
Bleeding Tendency in Jaundice	219
Purpura Hemorrhagica	221
Pregnancy	226
CHAPTER 10. ORGANIC DISEASES	229
Cardiac Disease	229
Minor Abnormalities	231
Major Abnormalities	235
Essential Hypertension	249
Nephritis	253
Renal Arteriosclerosis	253
Acute Glomerulonephritis	254
Chronic Glomerulonephritis	254
Examination of Urine	256
Renal Function Tests	257
Special Measures	259
Uremia	260
Diabetes	261
Preparation	262
Acidosis and Coma	269
Anesthesia	270
After Operation	271
CHAPTER 11. CHEMOTHERAPEUTIC AND ANTIBIOTIC DRUGS	275
Sulfonamides	276
Sulfanilamide	281
Sulfapyridine	287
Sulfathiazole	287
Sulfadiazine . . . .	290
Sulfamerazine	292
Intestinal Antisepsis	293
Sulfaguanidine . .	293
Sulfasuxidine . .	294
Sulfathalidine	295
Urinary Antisepsis. . . .	296
Sulfacetimide.	296
Penicillin	297
Administration . . . .	299
Dosage and Indications .	301
Streptomycin . . . .	306
Administration. . . .	307
Indications. . . .	309
Toxic Effects. . . . .	314

	Page
<b>CHAPTER 12. MINOR POSTOPERATIVE COMPLICATIONS</b>	317
Conjunctivitis	317
Pharyngitis	317
Bronchitis	319
Persistent Vomiting	320
Intestinal Distention	324
Urinary Retention	328
Urinary Tract Infection	337
Prophylactic Measures	337
Symptoms	337
Treatment	338
Hiccough	342
Skin	343
<b>CHAPTER 13. MAJOR POSTOPERATIVE COMPLICATIONS</b>	349
Postoperative Shock	349
Hemorrhage After Operation	350
Septicemia	353
Diagnosis	354
Treatment	354
Respiratory Tract Complications	358
Pulmonary Atelectasis or Massive Collapse of the Lung	359
Diagnosis	360
Prophylaxis	364
Treatment	367
Bronchopneumonia	372
Aspiration Pneumonia	374
Lung Abscess	375
Symptoms	375
Treatment	376
Thrombosis and Thrombophlebitis	377
Diagnosis	383
Prophylactic Measures	385
Treatment of Phlebothrombosis	387
Treatment of Acute Thrombophlebitis	397
Pulmonary Embolism	400
Symptoms	401
Prevention	404
Treatment	404
Subphrenic Space Infections	406
Symptoms	409
Localizing Signs	409
Treatment	410
Parotitis	410
Symptoms	410
Prophylactic Measures	411
Treatment	411
<b>CHAPTER 14. INTESTINAL OBSTRUCTION AND PERITONITIS</b>	415
Mechanical Intestinal Obstruction	415
Etiology	415
Pathology	417
Diagnosis	419
Treatment	424
Paralytic Intestinal Obstruction	439
Symptoms	440
Differentiation	440
Treatment	440

	Page
Peritonitis	442
Treatment . . . . .	446
Acute Gastric Dilatation.	451
Examination	451
Pathogenesis.	452
Treatment...	453
CHAPTER 15. CARE OF THE WOUND	455
Factors Influencing Wound Healing	457
Technique of Changing Dressings	459
Sutures . . . . .	463
Pressure Dressings	465
Infected Wounds.	469
Wet Dressings	470
Local Medication	474
Bactericidal and Bacteriostatic Agents	474
Digestants. . . . .	487
Growth-Stimulating Substances	488
Hemostatic Substances	489
Drains.	491
Wound Complications. . . . .	495
Postoperative Hemorrhage	495
Wound Infection.	496
Delayed Healing . . . . .	498
Dehiscence..	499
Gas Gangrene	503
Tetanus	507
Fistulas ..	511
CHAPTER 16. BURNS....	519
Pathology	519
Blood Changes.	522
Visceral Changes	522
Early Complications.	523
Treatment..	525
Treatment of the Burn.	525
Burns of the Extremities..	530
Burns of Other Areas . . . . .	531
General Treatment	531
Secondary Dressings	540
Skin Grafting	541
Infection	543
Diet.	545
Anemia	546
CHAPTER 17. THORACIC SURGERY	548
Physiologic Considerations. . . . .	548
Empyema . . . . .	550
Treatment. . . . .	552
Traumatic Wounds.	563
Lacerated Wounds....	561
Emergency Treatment..	565
"Wet Lung" . . . . .	566
Tension Pneumothorax..	567
Hemothorax..	568
Elective Surgery. . . . .	570
Special Preoperative Studies..	572
In the Operating Room...	576
Postoperative Care...	577

	Page
Pulmonary Resection for Suppurative Disease	583
Pulmonary Tuberculosis	591
<b>CHAPTER 18. STOMACH</b>	600
Preoperative Study	602
Preoperative Care	604
Postoperative Care	610
Diet	611
Total Gastrectomy	615
Postoperative Complications	617
Ulcer Complications	627
Ulcer Hemorrhage	627
Acute Perforation	630
Vagus Resection	633
Gastrostomy	637
Congenital Hypertrophic Pyloric Stenosis	639
<b>CHAPTER 19. SMALL INTESTINE AND APPENDIX</b>	641
Small Bowel	641
Preoperative Care	642
Following Operation	642
Enterostomy	643
Appendix	646
Interval Appendectomy	646
Acute Appendicitis	647
Appendicitis with Perforation	648
Appendical Abscess	649
Perforative Appendicitis With Generalized Peritonitis	652
<b>CHAPTER 20. LARGE BOWEL</b>	656
Ulcerative Colitis	656
Neoplasms of the Colon	661
Preparation for Operation	661
Operations	668
Care of Permanent Colostomy	678
Anus	680
Proctoscopic Examination	680
Preparation	681
Hemorrhoids	682
Fissure of Anus	686
Anorectal Fistulas	687
Pruritus Ani	688
Acute Infections	689
Plastic Operations	689
<b>CHAPTER 21. BILIARY TRACT</b>	692
Preoperative Care	692
Cardiovascular Disease	692
Kidney Function	692
Liver Function	693
Bile	694
Jaundice	695
Examination of the Blood	702
Improvement of Liver Function	702
Preparation of Jaundiced Patients	704
Hemorrhagic Tendency	705
Biliary Colic	707
Postoperative Care	709
Uncomplicated Cholecystectomy	710

	Page
Cholecystostomy. . .	711
Choledochostomy. . .	711
Complications Following Biliary Tract Surgery	717
Postoperative Hemorrhage . . .	717
Injury to the Common Bile Duct	718
Liver Failure . . .	720
<b>CHAPTER 22. THYROID</b>	724
Etiology of Hyperthyroidism . . .	724
Physiologic Effects of Hyperthyroidism	726
Preoperative Preparation	728
Physical Examination . . .	728
Primary Needs	729
Associated Heart Disease; Thyrocardiac Patients . .	739
Thyroid Crisis . . .	742
When to Operate	744
Postoperative Care . . .	745
Minor Complications . . .	747
Major Complications.	747
Thyroid Storm or Crisis	747
Respiratory Obstruction . . .	748
Pulmonary Complications.	750
Wound Infection	751
Parathyroid Tetany. . .	751
<b>CHAPTER 23. EXTREMITY</b>	756
Infections . . .	756
Peripheral Vascular Disease (Chronic Occlusive Arterial Disease)	758
History . . .	758
Physical Examination . . .	758
Diagnostic Tests . . .	761
Treatment . . .	763
Arteriovenous Fistula	773
Preoperative Studies	774
In the Operating Room . . .	776
Following Operation.	777
<b>CHAPTER 24. GYNÉCOLOGIC SURGERY.</b>	779
Preoperative Care . . .	779
In the Operating Room.	783
Postoperative Care . . .	784
Postoperative Complications	789
Postoperative Hemorrhage . . .	789
Pulmonary Atelectasis. . .	790
Phlebotrombosis, Thrombophlebitis, and Pulmonary Em- bolism . . .	790
Fecal Fistula. . .	791
Other Types of Fistulas . . .	792
Vesicovaginal Fistula. . .	794
<b>APPENDIX..</b>	797
Diet Lists. . .	801
Preparation for X-Ray Studies . . .	802
Cholecystography. . .	803
Gastrointestinal Series. . .	803
Barium Enema. . .	804
Oxygen Administration . . .	804
Indications. . .	804
Administration. . .	806



	Page
Infusions and Transfusions	812
Vacoliter Solution Administration Technique	812
Transfuso-Vac Blood Collection and Blood Transfusion Technique	815
Saftiflask Solution Administration Technique	823
Saftivalve Technique for Blood Collection and Transfusion	824
Intravenous Infusion Equipment	829
Collection and Administration of Blood Transfusions	831

# Preoperative and Postoperative Care of Surgical Patients

---

## CHAPTER 1

### GENERAL AIMS

Successful surgery often depends as much upon proper supportive care of the patient as upon technical operative skill. Care of the patient before and after surgery is planned to insure safe conduct through operation, prompt and complete recovery after operation, and effective prophylaxis and treatment of any untoward complications which may arise. In many cases, the supportive care is far more complicated and difficult than the operative procedure itself. There is actually no sharp dividing line between preoperative and postoperative care, the plan of preparation, the supportive measures required during operation, the operative procedure itself, and the management during convalescence are all coordinated into a unified program of treatment devised to fit the particular needs of the individual.

The condition of the patient is evaluated at the time of the initial examination; a complete history is taken and a thorough physical examination performed in every case without exception. Not infrequently another disease process entirely unrelated to the presenting illness will be found in the course of general examination and will radically alter the plan of therapy. The effects which the disease has produced upon the visceral functions of the body are studied in order to estimate the patient's acceptability for operation; measurement of the reserve capacity of the visceral organs is imperative when physiologic damage may be present or when an extensive operation is planned. In some cases, operation must be done even though visceral function is depressed; in others, the risk of operation is weighed carefully against the benefits to be expected from surgery.

When a major operation is contemplated or when the patient is in poor condition, enough laboratory tests and special studies

are made to permit confirmation of the diagnosis and reliable estimation of the operative risk. Such investigation must be thoughtfully planned; any test which will afford useful information should be ordered, but unnecessary tests may be confusing and are unduly expensive to the patient. It is a not uncommon practice to order a large series of miscellaneous tests in the hope of reaching a working diagnosis; such an approach is wasteful of time and money and is rarely of help.

A specific plan of management is devised in accordance with the patient's general condition, the operation to be performed, and the existence of complicating disease or physiologic derangements. Unless the nature of the disease permits no delay in treatment, enough time is allowed for preparation before operation to assure the patient a maximum chance for uncomplicated recovery. In many cases, if the patient is intelligent and co-operative, part of the preparatory treatment can be carried out at home under supervision. More often, the severity of the illness or the multiplicity of details of treatment will necessitate hospitalization. Although every effort should be made to improve the surgical acceptability of a poor-risk patient, it is not advisable to spend too much time in preparation. Early improvement is rapid under a well-planned program, but when a stationary level is reached and further progress becomes less evident, nothing can be gained by further postponement of operation. Patients with certain conditions (for example, severe hyperthyroidism, bronchiectasis, extreme obesity) may require unusually long periods of preoperative care. Unless such special indications for delay exist, however, undue prolongation of the preparatory period may result in deterioration of physical condition and discouragement of the patient.

Smoothness of convalescence depends to a great extent upon the conduct of operation. Preoperative sedation, expert induction of anesthesia, maintenance of anesthesia at the proper depth without overdosage, and well-informed postoperative care will help to reduce the incidence of postoperative pulmonary complications and, to some extent, of operative shock. Surgery performed with a minimum of trauma, without haste but without unnecessary loss of time, and the use of sharp dissection and fine suture material applied, whatever the type, with the "silk technique," will help to reduce the incidence of shock and of local

complications and to insure the success of the operation itself. For some years, it has been customary to begin an infusion at the start of every major operation, so that transfusions of blood may be given without loss of time if indications should arise. More recently, the demonstration that blood loss during certain operations is almost always significantly large has led to the practice of routine transfusion during extensive operations rather than after, with corresponding improvement in results.

Close watch is kept during the postoperative period for the earliest evidence of untoward incidents. Such potentially fatal complications as wound dehiscence, phlebothrombosis, or pulmonary embolism may produce nothing more than a slight sustained rise in temperature, pulse rate, and respiratory rate for a day or two, with no apparent cause. Minor degrees of fever or tachycardia therefore should not be considered lightly; the patient should be examined for additional signs or symptoms at least once daily, so that a diagnosis can be made and proper treatment instituted at the earliest possible moment.

Postoperative care does not end until the patient has been restored as nearly to normal health as his condition will permit. Such rehabilitation may require weeks or months of continuous therapy; a dietary plan is prescribed, with supplements as indicated, and the importance of steadfast observance of the diet and of the plan of medication is impressed upon the patient. The usual visit for postoperative checkup is made a month after operation; it is worth while also to request the patient to return for examination after six months have passed.

Before operation, either the patient or a responsible member of his family should be told of the tentative diagnosis and the nature of the proposed operation. In many cases, when the diagnosis is uncertain, it is well to secure permission to perform whatever procedure appears necessary at the time of operation. Following operation, the patient or his closest relative should be given a clear understanding of the postoperative diagnosis, the operation performed, and the prognosis. The question of what to tell the patient who has a malignant lesion, however, must be decided by the physician in accordance with the individual circumstances. Either the patient or the closest relative must be notified of the exact findings; if the situation has been discussed plainly with a responsible member of the patient's

family, it is often best to tell the patient enough to satisfy him but not enough to discourage him. Occasionally, there is no other choice but to be specific; more often, however, the patient will suspect the truth but will be grateful if he is allowed to retain some hope of cure or continued life.

## CHAPTER 2

# FLUID AND ELECTROLYTE BALANCE

### Physiologic Regulation

The fact that an individual's weight is maintained at so nearly a mathematically exact level, in spite of great daily variations in fluid and food intake, exercise, rest, and environment, indicates the perfection of the physiologic regulation of fluid and electrolyte balance. The importance of this regulatory mechanism in the reaction of an individual to a surgical operation cannot be overemphasized. Major metabolic disturbances, such as those following organic diseases and surgical procedures, always produce some alteration of the biochemical balances in the tissues. In order to insure as rapid a recovery as possible from the illness or surgical operation, the normal physicochemical relationships must be quickly restored and the fluid and electrolyte balances properly maintained. Recognition of certain fundamental principles is necessary.

Water represents approximately 70 per cent and blood plasma water about 5 per cent of the total body weight. Although the water content of the body is so great, it has been shown that loss of fluid equal to 6 per cent of the body weight will produce prostration and the picture of marked dehydration. A loss of this magnitude would approximate 9 pounds, or 4,000 c.c., in a patient weighing 150 pounds. This amount of fluid can easily be lost within one or two days by a surgical patient, for example, under adverse weather conditions or with a suction drainage tube in the gastrointestinal tract. With the same degree of fluid loss, an infant weighing 10 pounds would exhibit severe dehydration following a loss of only 275 c.c. of body fluid. Practically all aged patients and all patients suffering from affections of the gastrointestinal tract, as well as from diseases involving loss of appetite, evidence varying degrees of dehydration in addition to protein and vitamin starvation.

Close attention to and correction of disturbances of the fluid and electrolyte balance both before and after operation will often reduce to a low figure the mortality of an otherwise highly serious

operation. Since the reports of Donovan<sup>1</sup> and others, for example, the institution of proper fluid replacement therapy following prolonged vomiting in cases of hypertrophic pyloric stenosis of infants has decreased the mortality of the Fredet-Rammstedt procedure from 25 per cent to an almost negligible figure.

**Fluid Intake and Output.**—Fluid is normally taken into the body only by way of the mouth, either as fluid, intake of which is regulated by the sensation of thirst, or as food, which yields water as a chemical end product of metabolism. In calculations of fluid intake, the usual fluid foods may be considered for practical purposes to represent 100 per cent of their volume as available water. Solid food also yields water, both by virtue of its actual water content and because it produces water of metabolism as an end product. The total water yield of typical solid foods in the average diet amounts to about nine-tenths of the weight of the food. Total daily fluid intake therefore amounts roughly to a little less than the volume of fluids taken plus the weight of solid food eaten expressed as grams (or cubic centimeters) of water. Fluid intake should equal fluid output and must be maintained at an optimum level, which varies under different circumstances.

Fluid is lost from the body:

1. As water vapor in the exhaled air (about 300 c.c. daily).
2. As urine, the minimum daily output of which must be at least 600 c.c. and preferably 1,000 to 1,500 c.c., to prevent retention of nitrogenous end products.
3. By insensible evaporation from the body surface, amounting to 1,000 c.c. a day minimally.
4. As sweat, varying considerably with the circumstances.
5. In the feces, amounting to about 200 c.c. a day.

If the optimum urinary output is considered as 1,500 c.c. and if 1,500 c.c. daily is allowed for water of vaporization, fluid intake should average 3,000 c.c. to replace this loss in the absence of cardiac or renal disease. Since fluid loss by insensible evaporation, sweating, and exhalation is necessary to maintain proper regulation of body heat, the first evidence of insufficient fluid intake is seen as a decrease in the quantity of urine excreted.<sup>2,3</sup> The absolute minimum daily output of urine should be at least

600 c.c.; when the volume is this small, the urine must be concentrated in the kidneys to a specific gravity of about 1.030 in order to carry off the urinary solids, approximately 50 Gm. of which are normally excreted daily. If the total urinary output is less than 600 c.c., or if urinary concentration is impaired because of renal damage, nitrogenous end products and acid metabolites are retained in the blood. For the average adult, total daily urine therefore should be maintained by proper administration of fluids at an optimum quantity of 1,500 c.c., with a minimum of 1,000 c.c., in order to maintain a margin of safety.

This simple yet accurate criterion of proper fluid balance is usually sufficient for all practical purposes in the absence of cardiovascular or renal disease. Overenthusiastic forcing of fluids to a point beyond the power of the kidney to excrete the excess may result in waterlogging of the tissues and in pulmonary edema. These potentially fatal effects may be foreseen and avoided by maintaining the urinary output within the desired limits.

**Acid-Base Balance.**—The capillary walls are semipermeable membranes and the water and salts of the blood plasma and interstitial spaces diffuse back and forth, maintaining a constant equilibrium in the solute changes. Carbon dioxide and nitrogenous end products formed in the tissues enter the blood stream in this manner and their excretion is kept equal to production by means of respiration and kidney function. The ionic concentrations of plasma fluid, interstitial fluid, and intracellular fluid are the same and are approximately equivalent to the ionic concentration of normal (0.89 per cent) salt solution. Sodium is the chief basic ion outside the cell and potassium the chief base within, the sodium ions not diffusing appreciably across the cell membrane. It is evident, therefore, that when salt is retained in kidney disease, enough water must be held in the tissues to keep the salt at a proper physiologic concentration. With improved or stimulated kidney function diuresis occurs and salt and the excess fluid are excreted together.

**PULMONARY REGULATION.**—Oxygen and, to some extent, carbon dioxide are transported between the pulmonary and the systemic capillary circulations by the red blood cells, which therefore play an important part in regulation of the acid-base



balance of the body. Red blood cells, which have no nuclei and might perhaps be more accurately termed "corpuscles," are biconcave discs measuring approximately 7.0 microns in diameter, surrounded by a thin semipermeable membrane, and containing a stroma carrying the iron-containing pigment *hemoglobin*. The function of the red cell is to act as a carrier for hemoglobin, which transports oxygen from the lungs to the tissues at the average rate of 200 c.c. of oxygen per liter of blood.

Following inhalation into the lungs, oxygen diffuses into the capillaries of the pulmonary alveolar circulation and combines with the hemoglobin of the red blood cells to form oxyhemoglobin. Oxygen is liberated from oxyhemoglobin during passage through the systemic capillaries, where the oxygen tension is relatively low. On the venous side of the circulation, the hemoglobin therefore is in a partially reduced state, showing a lower oxygen saturation than the hemoglobin on the arterial side. The amount of this drop in oxygen saturation is proportionate to the degree of activity of the body tissues, locally as well as generally, and ordinarily amounts to about one-fourth of the total oxygen carried by the hemoglobin.

In addition to transporting oxygen to the tissues, hemoglobin plays an important part in the elimination of carbon dioxide. Hemoglobin is an amphoteric protein, acting as a weak acid in the oxidized state (oxyhemoglobin) and as a weak base when the oxygen content is reduced. Upon releasing oxygen in the systemic capillaries, the reduced hemoglobin therefore declines in acidity. Acting as a weak base, it combines with a portion of the carbon dioxide which has diffused into the blood stream from the body tissues and releases base or alkali radicals, previously held in loose combination by the weakly acid oxyhemoglobin. Extracellular alkali radicals, as mentioned previously, do not diffuse freely across cell membranes while anions do. The basic ions released by the reduced hemoglobin consequently remain within the cell but combine with bicarbonate ions and with chloride ions which diffuse into the red cells from the plasma. The plasma alkali formerly combined with these chloride ions is thereby freed to combine with carbon dioxide, forming additional bicarbonate. This mechanism is known as the *chloride shift* and is the way in which most of the carbon dioxide formed in the tissues is carried to the lungs for excretion. When the reduced hemoglobin

enters the pulmonary alveolar circulation, in which the oxygen tension is high, oxyhemoglobin is formed, the carbon dioxide within the red cell is given off, and the oxyhemoglobin again combines with the intracellular alkali ions. The chloride ions which had been held in the cell by the alkali then diffuse out into the plasma and displace an equivalent amount of the carbon dioxide held by the plasma alkali as bicarbonate. The released carbon dioxide passes out into the alveolar spaces and is exhaled.

The extreme pH range of the blood is from 7.0 to 7.6, with a normal average of 7.38 to 7.40. The hydrogen-ion concentration is kept within these narrow limits chiefly by the carbon dioxide buffer system of the blood and tissue fluids. Carbon dioxide normally present in the plasma as carbonic acid (acid in reaction) is approximately 3 volumes per cent and that normally present as sodium bicarbonate (alkaline in reaction) is about 60 volumes per cent. The carbon dioxide content of the blood is regulated by respiration with the utmost accuracy to maintain this ratio of 1 to 20 between the free carbonic acid and the carbonic acid bound as sodium bicarbonate (alkali reserve). Other buffer systems play a significant but less important role.

Nonvolatile and incompletely eliminated metabolic acids, such as lactic, sulfuric, and phosphoric acids, or excess acid metabolites formed, for example, in diabetes (beta-hydroxybutyric acid, amino-acetic acid), will displace an equivalent amount of bicarbonate in combining with sodium. This excess bicarbonate is excreted through the lungs as carbon dioxide, the excretion maintaining the ratio constant and thereby effectively buffering any pH change. The alkali reserve is decreased by exactly the amount of retained metabolic acid, the loss of available sodium impairing the carbon-dioxide carrying power of the blood. Deeper and more rapid breathing is necessary under these circumstances to eliminate the carbon dioxide produced in metabolism and the patient is said to be in acidosis. By a similar mechanism, loss of chloride ion without loss of sodium, as in persistent vomiting, will result in an increased formation of sodium bicarbonate and alkalosis may develop. In order to maintain a constant pH, the ratio of carbonic acid to bicarbonate is kept unchanged; carbonic acid is retained and the respiratory rate is diminished.

Carbonic acid, which keeps the blood alkali in very loose combination, is obviously a perfect buffer against sudden changes

in hydrogen-ion concentration, since it is continuously formed, is volatile, is a weak acid, and is easily eliminated through the lungs. It acts, however, only as a temporary expedient.

**RENAL REGULATION.**—More permanent correction of the displaced electrolyte balance is carried out by the kidney. Excess fluid is excreted, producing a urine of low specific gravity; on the other hand, if fluid intake is below normal, more fluid is reabsorbed in the tubules and a concentrated urine results. If nonvolatile acids in the blood stream are abnormally high, they are excreted by the kidney, but the sodium combined with them is partially retained. This retention of base is effected by endogenous synthesis of ammonia, which combines with the acid metabolite, and possibly also to some extent by the exchange of sodium ions for acid hydrogen ions.<sup>4</sup> The nonvolatile acid is excreted in the urine as the ammonium salt and, to a lesser degree, as the free acid, the sodium ion being retained as bicarbonate. The use of physiologic salt solution intravenously therefore will correct acidosis, the sodium chloride being retained and the excess acid being excreted as the sodium and ammonium salts; in this way the sodium bicarbonate reserve is rebuilt. Similarly, in alkalosis sodium chloride administered intravenously proves just as effective, the chloride ion being retained and the excess sodium being excreted as sodium bicarbonate. Finally, if the total solute is decreased, a dilute urine is excreted until the osmotic balance is re-established by means of relative dehydration. The functions of the kidney therefore include maintenance of proper fluid, electrolyte, osmotic, and acid-base balances.

Ingestion of large amounts of pure water results in excretion of the excess in the urine, necessarily with some sodium chloride in solution. Since the salt carried off in the urine is derived from the body store, a little fluid must be withdrawn from the tissues with the salt excreted in order to preserve normal osmotic relations. Administration of large quantities of water consequently may produce dehydration unless some salt is given in addition. If more pure water is taken than the kidneys are able to excrete, fluid is retained and the electrolyte and osmotic balances of the body tissues are disturbed. Water intoxication and sometimes even death may result.

The usual daily intake of sodium chloride on a normal average diet amounts to from 5 to 10 Gm., including both salt in the

food and salt added as seasoning. This quantity is sufficient to maintain proper salt balance in the tissues, except under conditions of abnormal salt loss. Salt ingested or administered in excess of this amount may be eliminated by normal renal excretion in quantities up to 20 to 25 Gm. in twenty-four hours. If more than this is taken or if an excess intake this large persists for more than a day or two, the excreting capacity even of normal kidneys will be overtaxed and salt will be retained in the tissues. A significant amount of excess retained salt will produce salt edema and salt intoxication. A proper balance of intake and output, charting both fluid and electrolytes given and amount and specific gravity of urine excreted, must be kept individually for each patient.

### Indications for Replacement Therapy

Since fluid intake is normally regulated automatically by the sensation of thirst, the first visible evidence of fluid deficiency is a dryness of the mouth, tongue, and lips. As a rule, simple dehydration without salt loss causes thirst, while loss of fluid with accompanying loss of salt is likely to cause weakness without thirst. The patient sometimes may be too ill to feel thirst and recognition of the fluid lack in such a case is the responsibility of the attending physician. Although the late stages of dehydration are obvious, the early evidences offered by parching of the lips, coating of the tongue, depression, apathy, and anorexia must not be ignored. Even these relatively early stages of dehydration will not develop if the precaution is taken routinely to measure and to record the daily urine output. Evidence of insufficient fluid intake will appear as a reduction of urinary output below 600 c.c. before any general manifestations develop.

Patients who are admitted in a possible state of dehydration and water and salt imbalance, or those who are suspected of developing this complication after operation, should be examined for abnormalities in the constituents of the blood and urine, which reflect every derangement of fluid and electrolyte balance.

**Examination of the Blood.**—Chronic disease, particularly of the gastrointestinal tract, is characteristically accompanied by *dehydration* because of the patient's disinclination to take food or fluids. Hemoconcentration accordingly develops and often

masks the anemia and hypoproteinemia which result from malnutrition. After fluid and salt deficiencies have been corrected, the true blood picture may be obtained, when the hematocrit and hemoglobin value will be found to be lower than at the time of admission and the plasma protein concentration will be at a depressed level. In some cases, chronic malnutrition will have reduced the plasma proteins below the point at which edema occurs, and restoration of the proper amount of fluid and salt then induces edema which did not appear earlier because of fluid lack.

Loss of chloride is evidenced by a drop in the plasma chloride (normally 550 to 650 mg. NaCl per cent). If the chloride ion alone has been lost and the sodium retained, as in vomiting due to pyloric obstruction, the freed basic ion will be found in combination with bicarbonate. Determination of the carbon-dioxide combining power of the blood shows it then to be greater than the normal of 50 to 65 volumes per cent because of the excess of base present and available for combination with carbonic acid (increased alkali reserve). If the loss of the sodium ion is greater than the loss of chloride, as in severe diarrhea or in the case of a pancreatic fistula in which base bicarbonate is lost, the carbon-dioxide combining power of the blood decreases concomitantly with the loss of the base. This is also true if metabolic processes are disturbed so that nonvolatile acid metabolites are produced, such as the ketone bodies formed in starvation or in diabetes mellitus. In these circumstances the organic acid forms a more stable combination with sodium than carbonic acid does and the carbon-dioxide combining power of the blood is decreased in exact proportion to the amount of ketone bodies present. These substances are usually present also in patients exhibiting simple dehydration and malnutrition and are formed as the result of starvation or, more specifically, as the result of increased oxidation of fats in the absence of a sufficient carbohydrate intake. Marked acidosis sometimes may cause a drop of the carbon-dioxide combining power to 30 volumes per cent or less.

**Examination of Urine.**—Dehydration, following insufficient fluid intake, usually is responsible for a decrease in urinary output. The urine in dehydrated patients with normal kidneys is concentrated to a specific gravity of 1.025 or higher and is dark in

color. If the total daily urine excreted is less than 600 c.c., urinary salts are retained in the body. Determination of the blood urea or nonprotein nitrogen under such circumstances shows a rise above the normal value.

If acidosis is present, ketone bodies are found in the urine, which shows an acid reaction to litmus. Alkalosis, on the other hand, is marked by the excretion of relatively large quantities of bicarbonate in the urine, which therefore is characteristically basic to litmus.

### Principles of Corrective Treatment

The average surgical patient in good general condition, undergoing the usual operative procedure from which an uneventful recovery can be expected, will come to the operating room in a satisfactory state of fluid and electrolyte balance and will recover without requiring special consideration or measures of treatment. As a rule, after the day of operation water is taken by mouth in small quantities, and a day or two later the intake of food and fluids begins to be sufficient in quantity to restore the loss suffered during the operative period. Such a patient may not need even a single dose of parenteral fluid.

More serious illnesses, more complicated and lengthy operations, and more complicated periods of convalescence will produce derangements in fluid balance, and corrective therapy will be required.

Reduced to simplest essentials, the daily water requirements for an adult amount to 1,500 to 2,000 c.c. for heat regulation (water of vaporization, insensible evaporation, perspiration) and to 1,000 to 1,500 c. c. for urinary excretion. Administration of a total of 2,500 to 3,000 c.c. of fluid (oral and parenteral) daily will ordinarily suffice. Adequacy of water intake can be checked simply and effectively by measurement of the total twenty-four hour output of urine, which should amount to not less than 1,000 c.c. and preferably 1,500 cubic centimeters. As an additional precaution, the specific gravity of the pooled specimen may be obtained to be sure that urinary concentration is in the middle range. If the output is too low, it is evidence that more fluid is required, and the difference between the actual and the optimum

(1,500 c.c.) day's urinary excretion is added to the preceding day's fluid intake, to be given the next day. For example.

FLUID INTAKE		FLUID OUTPUT	
Oral	1,100 c.c.	Urine	700 c.c.
Parenteral	1,500 c.c.		
Total	<u>2,600 c.c.</u>		
Optimum urinary output		1,500 c.c.	
Actual output		<u>700 c.c.</u>	
Deficit		800 c.c.	

The proper fluid intake for the following day will amount in this case to 2,600 c.c. plus 800 c.c., or 3,400 cubic centimeters. In a similar manner, fluid lost by gastric suction or biliary drainage is measured, and an amount equal to the quantity of drainage collected during each twenty-four hour period is added to the required fluid intake for the following day. On the other hand, if urinary output exceeds 1,500 c.c., a corresponding reduction in fluid intake may be made for the next day.

Fluid requirements usually are met by the administration of normal salt solution and dextrose (5 per cent) solution. Each of these solutions is approximately isosmotic with the blood and tissues, and either may be given intravenously. Dextrose solution is irritating to the tissues and in general should not be given by hypodermoclysis, although normal salt solution may be. Distilled water alone is unsatisfactory for parenteral use because it is not in osmotic balance with the body fluids and may cause irritation if given locally and hemolysis if given intravenously.

The daily requirement of sodium chloride will be satisfied usually by a single infusion of 1,000 c.c. of normal salt solution, which will supply 8.9 Gm. of salt. If there is a constant loss of chloride, as in a patient whose stomach or small bowel is being kept empty by means of a suction apparatus, an additional infusion of normal salt solution amounting to one-half the volume of fluid aspirated will replace the salt loss. The remainder of the fluid lost by suction drainage may be made up with dextrose (5 per cent) solution. The concentration of chloride ion in gastric and upper intestinal contents is about half that of normal salt solution, so that the salt lost in each liter of aspirated secretion will be compensated by the administration of 500 c.c. of physio-

logic salt solution. Further fluid requirements are met by the introduction intravenously of 5 per cent dextrose in distilled water in any quantity necessary to make up the estimated daily total.

In most cases, administration of more than 1,000 to 1,500 c.c. of normal salt solution daily is not only unnecessary, but is actually undesirable. Under normal physiologic conditions, the kidneys are able to excrete as much as 20 to 25 Gm. of sodium chloride daily in excess of the average requirement, but only for short periods of one or two days. Following anesthesia and surgical operation, however, renal function may be temporarily depressed, and salt will be retained. For every gram of excess salt, more than 100 c.c. of water will be held in the tissues to keep the osmotic relations constant. For this reason, administration of too much normal salt solution to a surgical patient will cause retention of fluid in the tissues with latent or evident edema, and in advanced degrees may even result in cardiac strain and pulmonary edema, perhaps literally drowning the patient. A slight excess of normal salt solution, given over a period of several successive days, will produce subclinical waterlogging of the tissues, with consequent interference with gastrointestinal digestive functions, wound healing, and convalescence. Retention of larger quantities of salt may cause marked edema of the viscera and of the lungs and may even give rise to large collections of fluid in the pleural and abdominal cavities.

A great deal of clinical and experimental work has been done on fluid and electrolyte balance by Coller and associates.<sup>5</sup> These authors advocated as a general rule for replacement of depleted sodium chloride in surgical patients that "for each 100 mg. per cent that the plasma chlorides need to be raised to reach the normal of 560 mg. NaCl per 100 c.c. the patient should be given 0.5 gram of sodium chloride per kilogram of body weight." Further investigation by the same group apparently has shown, however, that this clinical rule, which has gained wide acceptance since its proposal, is not without danger, and its use is no longer advocated. The rule was devised on the basis that the concentration of plasma chloride is always directly dependent upon the tissue fluid volume and that the concentration of plasma chloride is in a fixed ratio to the concentration of the sodium ion. Coller<sup>6</sup> and co-workers point out in a more recent article that



since the plasma chloride can vary independently of the body water as a result of variations in other plasma anions, the rule devised for replacement of abnormally lowered plasma chloride can no longer be advocated, and fluid and electrolyte replacement should be calculated clinically only on the basis of immediate fluid needs and physiologic response to each day's fluid supply.

These authors have stated further that patients in the early postoperative period sometimes exhibit "salt intolerance" and are unable to excrete salt given during this time. They therefore recommend that following general anesthesia and operation no salt, not even in the form of normal salt solution, should be given for the subsequent forty-eight hours in the average case. During this time, fluid balance should be met by oral or intravenous introduction of dextrose (5 to 10 per cent) in distilled water. On the other hand, evidence has been brought forward by Ireneus<sup>7</sup> that marked restriction or loss of chlorides sometimes may induce symptoms similar to those produced by salt edema. Characteristically this condition is likely to occur in patients with fistulas or obstructions of the upper gastrointestinal tract with extensive loss of chloride without replacement. Despite the similarity in symptoms, hypochloremia may be differentiated from salt accumulation by the presence of a low level of plasma chloride and by the absence of edema. Ireneus feels that while salt-containing fluids may be withheld advantageously during the first few postoperative days, certain patients will develop hypochloremia during this period and will require prompt diagnosis and immediate sodium chloride replacement therapy according to Coller's originally advocated clinical rule. Further investigations on this subject are being carried out.

**Summary.**—The simplest plan to follow in maintaining proper fluid balance in the great majority of surgical patients is to estimate and administer their average daily basic fluid requirement (2,500 to 3,000 c.c.), to make certain of its adequacy (total daily urine output of 1,000 to 1,500 c.c.), and to supply extra fluid in a volume-for-volume replacement for all body secretions (except urine) or exudates lost through suction or drainage. For the first day or two after operation, fluid should be supplied

as dextrose (5 per cent) solution, and thereafter 1,000 c.c. of the daily fluid requirement may be given as normal salt solution. Additional fluid sufficient to replace lost secretions or aspirated material may be given as normal salt solution and dextrose (5 per cent) solution in equal quantities. If untoward symptoms should develop without edema, determination of the plasma chlorides will indicate whether hypochloremia is responsible; if such symptoms develop with edema, salt intoxication is more likely and also can be diagnosed by determination of the level of chloride in the blood.

If *acidosis* is present, normal salt solution will correct the electrolyte imbalance, the sodium and chloride ions being retained and the metabolic acids and salts being excreted by the kidney. Not over 1,000 c.c. of salt solution should be given at one time, although dextrose solution (5 to 10 per cent) may be used to supply additional needed fluid as well as carbohydrate to combat ketosis. Acidosis of severe degree causes a significant reduction of the alkali reserve, the metabolic acids combining with sodium and the chloride ion remaining unchanged. Because of this increase in strong acid ions, Hartmann's solution, which contains sodium lactate as well as sodium chloride, is somewhat more appropriate in treatment of acidosis than is normal salt solution, which contains only sodium chloride. In advanced or severe acidosis, one-sixth molar solution of sodium *r*-lactate (containing 18.66 Gm. of sodium *r*-lactate per liter) is preferable, about 10 c.c. of the solution per kilogram body weight being sufficient to elevate the carbon-dioxide combining power of the blood by 10 volumes per cent. While the approximate amount required in any specific case can be determined in this manner if laboratory facilities are available, it is also safe simply to administer 500 to 1,000 c.c. of the solution to an adult in severe acidosis, or 10 c.c. per pound of body weight to an infant. Sodium *r*-lactate solution is administered only for the treatment of moderate to severe acidosis or to alkalinize the urine in case of sulfonamide toxicity or for prevention or treatment of hemoglobinuria from transfusion reaction or crushing injury.

Recent work<sup>5</sup> appears to indicate that a significant amount of potassium is lost from the intracellular fluid compartment in conditions such as infantile diarrhea, which causes dehydration with acidosis. Improved clinical results<sup>6</sup> have followed addition

of potassium salts to the fluid administered for replacement therapy. However, since potassium in excessive amounts is likely to cause severe toxic symptoms, including progressive cardiac ventricular block, its use in clinical treatment of dehydration and acidosis is not yet generally advisable.

*Alkalosis* may be treated satisfactorily by the administration of normal salt solution, sodium bicarbonate being excreted in the urine and sodium chloride being retained. When the proper balance has been reached, the excess salt simply is excreted as such. When alkalosis is present, the use of Hartmann's solution or of sodium lactate solution is strongly contraindicated.

Protein deficiency requires the use of human blood, plasma, serum, or concentrated serum albumin transfusions for correction or improvement that must be achieved within a relatively short period of time. Treatment of malnutrition or more gradual correction of tissue and plasma protein deficiency may be accomplished by means of a high protein diet or by the use of protein hydrolysates given either intravenously or orally or both. If solutions of crystalloids alone are used as infusions in patients exhibiting protein deficiency, tissue edema will result, since the excess salt-containing fluid decreases the intravascular osmotic tension and fluid is forced out into the tissues.

### Complications of Fluid Therapy

Administration of salt beyond the renal power of excretion will result in salt and water retention, at first with latent edema, then generalized body waterlogging, and finally pulmonary edema. This condition may be relieved simply by discontinuing administration of salt solution and substituting 5 per cent dextrose, the sugar being metabolized and the water acting as a diuretic. Fifty per cent dextrose or sucrose solution given intravenously in quantities of 50 to 100 c.c. also will induce diuresis, fluid being withdrawn from the tissue spaces into the blood stream, whence it is excreted by the kidneys. The hypertonic sugar solution appears also to have a direct stimulating action on the kidneys and on the myocardium. Sucrose is probably somewhat more effective, since it is not metabolized. Sucrose should not be administered intravenously to patients with kidney disease, since it is likely to induce renal irritation.

In the presence of cardiac or renal disease extreme care is necessary to avoid overtaxing the diminished capacity of the damaged organ by administration of excess fluids. Parenteral fluids given too rapidly or in too large quantities may precipitate heart failure even in a well-compensated cardiac patient. The sudden or unexpected appearance of cardiac asthma in a subject of this type who has been receiving intravenous fluids may indicate an early pulmonary edema; examination of the lungs may show physical findings resembling those characteristic of pneumonia. Administration of a diuretic such as hypertonic sugar solution (25 to 50 per cent) intravenously in doses of 50 to 75 c.c. and discontinuance of excessive fluid administration are usually all that are required to correct the condition.

### Administration of Fluids

The fluid requirement, as previously stated, varies in type and amount with the individual and his disease. Some illnesses prevent administration of fluid by mouth and other routes must be chosen.

**Proctoclysis.**—Normal salt solution or tap water may be given slowly per rectum by means of a rectal tube and a funnel. Amounts of 100 and 250 c.c. are used, depending on the weight of the patient, and may be repeated every six hours for not more than three days. After this length of time a mild irritation of the rectum usually develops and the fluid is expelled as soon as given. All solutions administered in this manner should be heated to 100° F.

For administration of larger amounts of fluid per rectum, a *Murphy drip* (Fig. 1) may be used after the lower bowel has been cleared by an enema. This apparatus permits a slow continuous flow and is usually adjusted to deliver about 40 to 60 drops per minute. Use of a small soft catheter passing under the thigh and fastened to it by adhesive tape is preferable to a rectal tube. Rectal distention and expulsion of the fluid frequently occur within forty-eight hours or less and the drip must be discontinued.

In general, proctoclysis is not very efficient and is annoying to the patient.

**Hypodermoclysis.**—Normal salt solution or Ringer's solution may be given subcutaneously in amounts of 1,000 c c daily. This route of administration is used most commonly in the treatment of simple dehydration when the superficial veins are difficult to puncture and are being saved for transfusions or intravenous medications. An intravenous set is used, with an 18-gauge infusion needle (Fig. 1).

The fluid may be administered either subpectorally or in the outer thigh. For subpectoral administration, the needle is inserted at the lower outer edge of the pectoral muscle and is directed upward toward the axilla. Hypodermoclysis in this area is inconvenient and painful to the patient, and there is a very real danger that the thoracic cavity may be entered with the needle, especially in a thin individual. Pain on respiration suggests that the needle has penetrated an intercostal space and is in contact with the lung or pleura. Rapid flow of the fluid from the bottle or tubing indicates that the solution is pouring into the pleural cavity and the needle, of course, should be withdrawn instantly. A second hazard of hypodermoclysis in this location is the inadvertent introduction of the needle into the tissues of the breast in the female. The entire gland may become painfully distended and waterlogged and, if a small blood vessel is damaged, may develop a spreading hematoma. In a small thin patient, care must be taken to avoid the axillary vessels. The second and preferred site is on the outer thigh midway between the trochanter and knee, with the needle inserted upward. The needle may be introduced at an angle of 30 degrees, to rest just above the fascia lata, or at a 45-degree angle, to rest just beneath it. Either angle is satisfactory.

The area selected should first be cleaned with iodine and alcohol and the site of puncture anesthetized with procaine, 1 per cent. After the needle is inserted, the hub and the lower end of the tube are fastened to the thigh with adhesive tape and covered with a sterile dressing. The amount of fluid absorbed depends on the state of the patient's circulatory system and the flow should not be rapid enough to produce painful distention around the needle. Local swelling develops rapidly in cachectic patients and this mode of fluid administration may have to be abandoned. Marked distention around the needle prevents absorption and

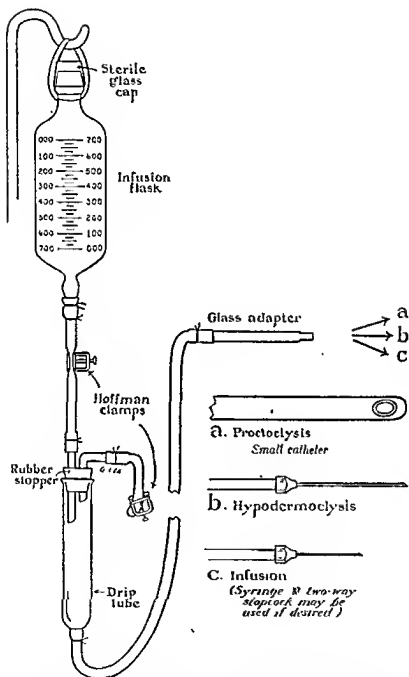


Fig. 1.—Apparatus for administration of fluid by various routes. Rate of flow is adjusted by the Hoffman clamp above the drip chamber. Level of fluid in the drip chamber can be regulated by opening the clamp on the air vent. Intravenous medications can be added in small amounts by puncturing the rubber tubing with a hypodermic needle. The use of commercial infusion apparatus is described in the Appendix (p. S12).

often encourages the development of an abscess or of deep phlebitis.

Ordinarily a liter of fluid may be administered by this route each day. If the needle becomes clogged, the treatment should be discontinued and a fresh one started in the opposite leg. The apparatus must not be allowed to run dry at any time. Dextrose or sodium bicarbonate solutions are not advised for subcutaneous administration because of their irritating properties. Hypodermoclysis is becoming less popular, since it is more painful and less certain than venoclysis and since it is sometimes followed by a widespread slough.

In infants single doses of 50 to 75 c.c. of normal salt solution may be given subcutaneously in the loose tissues between the scapulas and in the buttocks. The solution is administered by syringe and needle and injection may be repeated as often as required. Hypodermoclysis also is quite satisfactory in infants.

**Intravenous Fluids.**—Venoclysis (Fig. 1) is usually the method of choice for parenteral administration of fluids. Dextrose (5 per cent), normal salt solution (0.89 per cent), and Ringer's solution all are approximately isotonic with the blood and may be given intravenously in doses of 500 to 1,000 c.c. at a time, either singly or combined in any proportion desired. Several doses may be given at equally spaced intervals throughout the twenty-four hours to assure the average total daily fluid intake of 2,500 to 3,000 cubic centimeters. Administration of infusions, particularly of dextrose solution, should be slow. If more than 20 Gm. of dextrose (400 c.c. of 5 per cent dextrose solution) is administered per hour, the carbohydrate will not be fully metabolized but will be partially lost in the urine. Isotonic fluids ordinarily may be given intravenously in 500 c.c. doses within a period of one hour, although they must be administered much more slowly and cautiously to cardiac patients.

It may be stated parenthetically that sugar administered by mouth in those patients who are able to take it is probably as effective as sugar given intravenously, as Althausen<sup>10</sup> has shown. Absorption of carbohydrate from the intestinal tract takes place so slowly that the blood sugar is not ordinarily raised beyond the level at which sugar is lost in the urine. Dextrose solution administered intravenously sometimes is given so

rapidly that the rate of glycogen synthesis is exceeded and much of the sugar is lost by excretion into the urine. Both routes, however, are equally effective if the rate of intravenous administration is slow enough to permit complete utilization of the carbohydrate. This investigator points out that choice of route for simple carbohydrate administration therefore is a matter of convenience, unless vomiting or disease of the gastrointestinal tract is present.

Administration of an infusion requires a certain amount of skill and attention to detail on the part of the operator. All the air should be removed from the apparatus by alternately raising and lowering the bottle with the needle open. Care must be taken not to contaminate any of the connections if the needle becomes clogged during use and must be replaced and reinserted. During administration of the infusion, a responsible person must watch the set closely to make sure that the needle does not come out of the vein and that the reservoir does not run dry; in some hospitals an attendant is required to remain with the patient while an infusion is being given.

Superficial veins of the extremities are ordinarily used. If the infusion is given in the forearm, a vein in the middle or lower third is preferable to one near the elbow. Sudden flexion of the arm may force a needle in an antecubital vein through the opposite wall of the vessel, with resultant extravasation into the tissues. If the superficial veins of the antecubital fossa and the surface of the forearm are not available for use, a satisfactory vein usually can be found on the lateral aspect of the forearm, proximal to the radial styloid. This vein, as well as the veins on the back of the hand, is located beneath tougher skin and is relatively mobile. Venipuncture in these areas therefore requires somewhat more care. In the lower extremity, the anterior saphenous vein just anterior to the medial malleolus is most suitable for venipuncture, although veins on the dorsum of the foot sometimes are sufficiently large. When veins are scarce, puncture is done as far distally as possible, since a tear in the proximal portion of a vein temporarily prevents use of its distal portion for administration of fluid.

The tourniquet, preferably a blood pressure cuff, is applied several centimeters above the point selected for puncture rather than at a considerably higher level. The vein is allowed to fill



until it is firmly engorged with blood; attempts to puncture a partially filled vein usually result in formation of a hematoma. If satisfactory filling does not take place, the extremity may be allowed to hang down over the edge of the bed while the patient alternately flexes and extends the hand or foot. Application of hot wet towels or hot water bottles to the entire extremity almost always will increase the venous flow sufficiently to permit venipuncture.

The selected site is cleaned with an appropriate antiseptic. The operator exerts downward traction on the skin with his left thumb to immobilize the vein and inserts the needle through the skin just to the side of the vein rather than directly above it. The wall of the vein is engaged with the point of the needle, which is then pushed gently into the lumen of the vein and is carried forward carefully for a distance of 1 centimeter. As blood flows back through the needle, the tourniquet is released and administration of fluid is begun. Large veins permit use of 19 gauge needles; small veins require small (20 to 21 gauge) needles. The needle is inserted with the bevel up in large veins, but should be introduced with the bevel down in small veins to prevent tearing of the opposite wall. After the needle is in place, a folded sponge is placed beneath the hub to keep it at the proper angle, and it is fixed in place with a strip of tape (Fig. 2). Another strip of tape is placed across the glass adapter and a third strip attaches the infusion tubing to the skin of the extremity.

While the method of choice for venoclysis is the administration of fluid in divided doses of 1,000 c.c. at different times during the day, some authorities favor the use of *continuous intravenous infusion*, especially when relatively large quantities of fluid must be given parenterally over a period of several days. The amount of fluid given by continuous infusion must never be so large or so rapidly administered that it will overtax the circulatory or cardiac reserve of the patient. The quantity and types of fluid used are determined and regulated accurately by the calculated need of the individual in order to meet the physiologic requirements.

A continuous infusion, regulated at 50 drops per minute, will deliver 3,000 c.c. of fluid in twenty-four hours. An ordinary infusion apparatus may be used, but extra care is necessary in splinting the extremity securely and in strapping the needle in

place. This method, which has had wide popularity in the past and is still in general use, is subject to the minor disadvantages that the needle may clog frequently or may pull out of the vein. The chief disadvantage is that excessive amounts of fluid may be given unless care is exercised to maintain the hourly rate of flow at exactly the proper point.

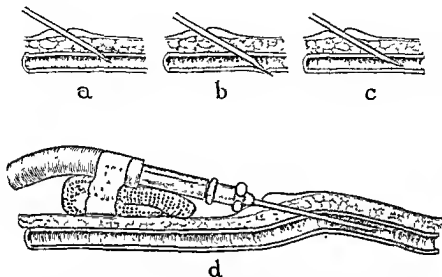


Fig. 2.—Venipuncture in a small vein. Long-bevel needle with bevel up may permit, *a*, leakage or, *b*, puncture of the opposite wall, with resulting hematoma. A sharp short-bevel needle is preferable. Introduced, *c*, with the bevel down. Needle is passed gently into the lumen of the vein for about 1 cm. and taped in place, *d*, with a sponge beneath the glass adapter to prevent kinking of the vein.

A *cannula* connected with the intravenous set (Fig. 3) is less likely to be displaced than a needle, but it is a great deal more difficult to insert. Any of the superficial veins in the extremities is suitable for the insertion, but the most suitable vein is the anterior saphenous, located a little anterior to the internal malleolus. If this vessel is to be used, the technique is as follows: the area is cleaned, draped, and anesthetized with procaine; a transverse or oblique incision 1.5 cm. in length is made, allowing adequate exposure of the vein, which is dissected free and elevated by means of two silk ligatures passed beneath it. The distal ligature is tied around the vein as low as possible, a small opening is cut in the anterior venous wall above the ligated area, and the cannula is inserted and tied in place with the second

ligature (Fig. 3). Some prefer to leave the incision open, but it is probably better to close the ends at least. A dressing is applied and is used as a support for the cannula, which is further im-

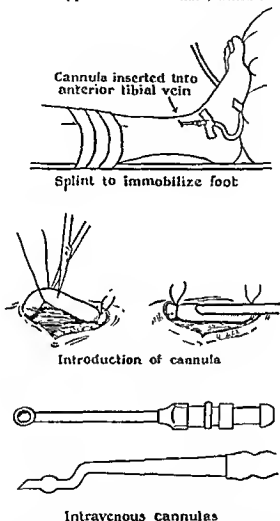


Fig 3—Continuous infusion. Cannula is held in vein by a ligature distal to the flange. Foot is supported to prevent foot drop. Fine plastic tubing for cannulation also is highly satisfactory.

mobilized with adhesive. The tube is then carried beneath the foot and is strapped to the skin in several places with enough slack to avoid tension and to prevent any tendency for the can-

nula to pull out. If an arm vein is used, a board splint should be applied to prevent flexion.

If a cannula is employed, administration of fluid may sometimes be continued for from two to four days, but it usually is necessary to discontinue it before that time. Frequently the cannula becomes clogged or is pulled out or the vein may become thrombosed. Other possible complications include significant wound infection, ascending thrombophlebitis, introduction of air into the veins, and embolism with the danger of pulmonary infarction or pneumonia. Repeated single doses given intravenously or a continuous intravenous drip through an ordinary venipuncture will supply almost as much fluid, cause less trouble, and prove much safer.

Although it is customary to warm the solutions to body temperature before administration of an infusion, it is not necessary. The use of cold solutions is rarely followed by untoward results of any kind; in fact, reactions are more likely to occur if the solution is warmed before administration either by immersing the flask in hot water or by placing the lower portion of the infusion tubing between two hot-water bottles. The fluid may be heated to a point considerably above body temperature by this procedure, and an infusion reaction may ensue.

Infusion reactions, evidenced by an immediate chill and a transitory temperature rise of several degrees, usually are due to pyrogens, which are products of bacterial growth or decomposition forming in previously used tubing or glassware that was not promptly or adequately cleaned immediately after use. Reactions of this type are no longer common, both because of more widespread use of commercially prepared and sterilized solutions and apparatus and because of improved technique<sup>11</sup> in preparation of fluids and apparatus in hospitals which make up their own solutions.

**Intraperitoneal Transfusion.**—Administration of blood<sup>12</sup> or of other fluids to infants by intraperitoneal transfusion was formerly advised when venipuncture is particularly difficult. It is questionable, however, whether absorption of blood from the peritoneal cavity is sufficiently rapid and complete to make this route of transfusion satisfactory. Because of the uncertainty of absorption and the possibility of accidental wounding of the in-

testine, intraperitoneal transfusion or infusion is no longer widely used.

**Intramedullary Administration.**—Intramedullary administration of fluids and blood has been advocated by Tocantins and O'Neil<sup>13</sup> since 1940 following their demonstration that such fluids introduced into the marrow cavity of bones are absorbed completely and fairly rapidly without change. Further use of the method<sup>14</sup> has indicated that while it is often useful and effective, it is not without some danger. It is advised, therefore, only when intravenous injections of fluid or blood are indicated and the peripheral veins are too damaged for satisfactory use. Intramedullary injection of fluids should be done only by those familiar with the technique and the possible complications that may result from its improper employment. Necessity for use of this route does not arise very often, most clinics preferring puncture of the scalp, anterior saphenous, or external jugular veins in an infant or operative exposure of a superficial vein in a patient of any age, with introduction of a needle or cannula under direct vision.

The manubrium and the center of the body of the sternum are the preferred sites in adults and in children over 4 years of age, while the upper tibia and lower femur are preferred in infants and in children under 4 years. The sternum is not used in infants because the marrow cavity is too small and the risk of entering the thoracic cavity too great. The long bones are not used in older children or adults because the cortex is too thick and the marrow more dense.

Specially designed needles are usually employed.<sup>14</sup> For sternal puncture<sup>15</sup> in adults, the proper site on the manubrium or sternum is cleaned and anesthetized by infiltration with procaine (1 per cent) down to and including the periosteum. The completely assembled needle is introduced vertically through skin and periosteum, with the bevel up (Fig. 4). When the point is in contact with bone, the needle is pointed cephalad to make an angle of 30 degrees with the sternum and is passed through the anterior plate of the bone into the marrow cavity by application of pressure with a twisting motion. The needle guard then is adjusted to maintain contact with the skin to prevent further entry of the needle. The stylet is removed, a syringe containing a

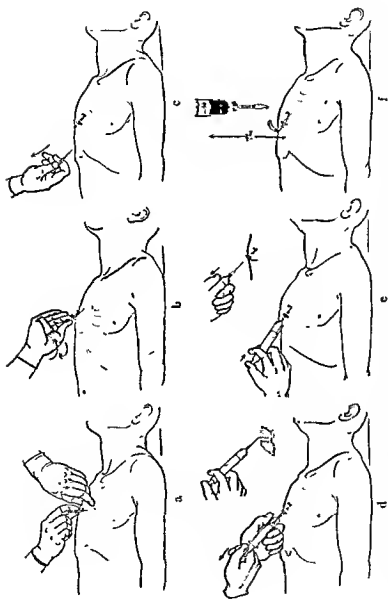


Fig. 1—Technique for intramedullary infusion in the sternum. a. Penetration of skin, subcutaneous tissue and pericostum, b. entering the bone and marrow, semirotatory motion, c. removal of stylet adjustment of guard d. aspiration of marrow. (Inset flushing out internal needle) e. reinsertion of needle, injection of saline (inset, removal of internal needle), f. connection to infusion gravity apparatus (From Tocantins and O'Neil Surg. Gynec & Obst. 73: 251, 1931.)

little sterile normal salt solution is attached to the inner needle, and gentle suction is applied. If the needle is properly placed within the marrow cavity, a pink tinge of blood and marrow will appear in the syringe. All the air is removed from the inner needle attached to the syringe by withdrawing it, forcing several drops of salt solution through it, and reinserting it into the outer needle, which was left in place. Several cubic centimeters of salt solution are again expressed from the syringe to empty the air from the outer needle. A small quantity of solution then is expelled slowly into the marrow cavity to make sure the position of the needle is correct. The syringe and inner needle again are withdrawn and the tubing of the infusion apparatus, from which every bubble of air has been expelled, is attached to the end of the heavy needle. All these steps should be done fairly quickly to avoid clotting in the needle. The infusion is begun.

In infants, the sternum is not used; the sites advised are the anteromedial aspects of the metaphyseal regions in the upper tibia and lower femur. The upper tibia probably is preferable, and the procedure is performed<sup>13</sup> in the same manner as sternal puncture. The baby's ankle and knee are fastened to a well-wrapped board splint firmly but without compression of the circulation. For penetration of the cortex, the needle is tilted to an angle of 60 degrees with the horizontal rather than 30 degrees and is directed away from the knee to avoid penetration of the epiphysis (Fig. 5). Short needles are used in infants,<sup>14</sup> the shaft measuring not over 2 cm. for tibial puncture and 4½ cm. for femoral. An ordinary 19 gauge (½ inch) needle also is satisfactory for infants under 6 months of age and an 18 gauge (1 inch) needle for those who are older.

The needle may be left in position for as long as twenty-four hours in an adult but should not remain more than twelve hours in an infant. The bottle is elevated about three feet above the level of the needle. The rate of flow is limited by the density of the marrow and the size and age of the patient but can probably be adjusted to deliver from 1.5 to 4 c.c. of aqueous solutions per minute. Fluids with greater viscosity flow at a slower rate; the rate of flow of plasma will approximate 1.0 to 2.0 c.c. per minute, while blood will be absorbed only at the rate of 0.5 to 1.0 c.c. per minute. Efforts to administer whole blood by intraosseous transfusion sometimes are completely unsuccessful.

Liquids suitable for intramedullary administration include whole blood, plasma, normal salt solution, and 5 per cent dextrose in distilled water. Drugs, such as soluble sulfonamides, penicillin, and crystalline vitamin solutions, may be added to the infusion. Oily preparations are not suitable for intramedullary administration, even in small quantities.

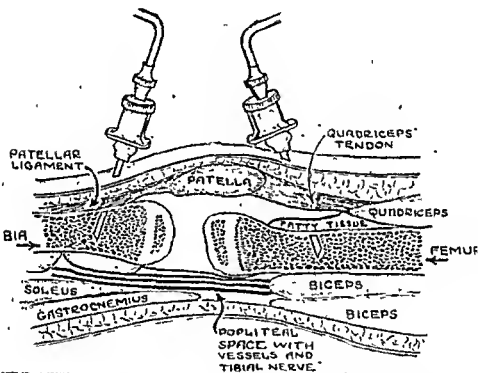


Fig. 5—Diagram of a longitudinal section of the knee joint area in a full-term, newborn infant, showing the important anatomic relations and the correct position of needles for infusion. In the diagram the size of the joint cavity proper is purposely exaggerated. (From Tocantins and O'Neill. *Ann Surg* 122: 266, 1945; J. B. Lippincott Co.)

Meola<sup>16</sup> suggests the use of a 1.5 inch, 18 gauge Kalinski salvarsan needle for use in children under 2 years of age and a B-D Special Needle No. 458 L.N.R., gauge 16, in children from 2 to 4 years of age. With the technique Meola advocates, the appropriate needle is simply attached to a 5 c.c. syringe containing a little normal salt solution and under sterile conditions is pushed slowly into the marrow cavity of the tibia or femur at the proper



site. Aspiration is done to be sure that the needle is properly placed in the marrow cavity, after which the small syringe is replaced with a larger one. The entire infusion is given by injecting the fluid through the syringe under gentle pressure at a slow rate. Only one reaction and one complication were reported by Meola in a series of 326 intramedullary infusions, with no unsuccessful attempts.

Certain precautions are advisable: (1) The sternum and manubrium are not used in patients under four years of age. (2) The upper tibia and lower femur are not used in patients over 4 years of age. (3) Undue pressure on the needle is avoided to prevent penetration of both plates of the sternum or of both cortices of the tibia or femur. (4) If a sternal puncture is unsuccessful, a second attempt should not be made near the first site of puncture for at least twelve hours, to avoid leakage through the first puncture site. (5) If the entire sternum is pierced, it is inadvisable to draw the needle back into the marrow cavity and begin the infusion. Leakage may occur through the perforated posterior plate into the mediastinum. (6) If a sternal infusion is repeated within less than twelve hours, the second puncture should be made at least 6 cm. away from the first. (7) No infusion should be begun until it is certain that the needle is in the proper position in the marrow cavity as evidenced by appearance of a pink tinge on aspiration, indicating blood and marrow. (8) Care must be taken that the needle does not become dislodged, with resultant accumulation of fluid under pressure in the subcutaneous tissues.

The chief complications include leakage of fluid into the mediastinum with resulting mediastinitis, leakage into the pleural cavity with resulting pulmonary collapse or pleural infection, or leakage into the subcutaneous tissues with resulting pressure necrosis, cellulitis, or osteomyelitis. The method obviously is not applicable to patients suffering from local infections near the proposed site of puncture, from blood stream infections, or from osteomyelitis.

### References

1. Donovan, E. J.: Congenital Hypertrophic Pyloric Stenosis in Infancy, *J. A. M. A.* 109: 558, 1937.
2. Maddock, W. G., and Colfer, F. A.: Water Balance in Surgery, *J. A. M. A.* 108: 1, 1937.

3. Coller, F. A., Dick, V. S., and Maddock, W. G.: Maintenance of Normal Water Exchange With Intravenous Fluids, *J. A. M. A.* 107: 1522, 1936.
4. Pitts, R. F., and Alexander, R. S.: Nature of Renal Tubular Mechanism for Acidifying Urine, *Am. J. Physiol.* 111: 239, 1945.
5. Coller, F. A., and others: Replacement of Sodium Chloride in Surgical Patients, *Ann. Surg.* 108: 769, 1938.
6. Coller, F. A., Campbell, K. N., Vaughan, H. H., Iob, L. V., and Moyer, C. A.: Postoperative Salt Intolerance, *Ann. Surg.* 119: 533, 1944.
7. Ireneus, C., Jr.: Hypochloremic State in Surgical Patients, *Surgery* 18: 582, 1945.
8. Darrow, C.: The Retention of Electrolyte During Recovery From Severe Dehydration Due to Diarrhea, *J. Pediat.* 28: 515, 1946.
9. Govan, C. D., and Darrow, D. C.: The Use of Potassium Chloride in the Treatment of Dehydration of Diarrhea in Infants, *J. Pediat.* 28: 541, 1946.
10. Althausen, T. L.: Deposition of Glycogen in Normal and in Experimentally Damaged Livers After Oral and Intravenous Administration of Dextrose, *Am. J. Digest. Dis. & Nutrition* 1: 752, 1938.
11. Walter, C. W.: The Relation of Proper Preparation of Solutions for Intravenous Therapy to Febrile Reactions, *Ann. Surg.* 112: 603, 1940.
12. Ravdin, I. S., and Johnston, C. G.: The Use of Continuous Intravenous Infusions in Acute Abdominal Crises, *Ann. Surg.* 97: 749, 1933.
13. Tocantins, L. M., and O'Neil, J. F.: Complications of Intra-Osseous Therapy, *Ann. Surg.* 122: 266, 1945.
14. Tocantins, L. M., O'Neil, J. F., and Jones, H. W.: Infusions of Blood and Other Fluids Via Bone Marrow: Application in Pediatrics, *J. A. M. A.* 117: 1229, 1941.
15. Tocantins, L. M., and O'Neil, J. F.: Infusions of Blood and Other Fluids Into General Circulation Via Bone Marrow, Technique and Results, *Surg., Gynec. & Obst.* 73: 281, 1941.
16. Meola, F.: Bone Marrow Infusions as Routine Procedure in Children, *J. Pediat.* 25: 13, 1944.

## CHAPTER 3

### METABOLISM AND NUTRITION

Because of the great importance of many of the recent advances in clinical physiology, an appreciation of the fundamentals of metabolism is invaluable to the surgeon. It is no longer necessary to depend entirely on feeding by mouth, with supplementary transfusions of blood or of plasma, to restore or maintain a sick patient's nutritional balance. Even though oral feeding is preferable, fluid, minerals, vitamins, carbohydrates, predigested or hydrolyzed proteins, supplementary pure amino acids, blood, and plasma can all be given parenterally in sufficient quantity to enable an undernourished patient to gain weight. The only major dietary factor not yet generally available for parenteral administration is fat, and even this has been given clinically in several cases. As a basis for working out and apportioning properly a balanced and optimum plan for feeding a patient unable to take sufficient food or fluid by mouth, some of the principles of metabolism and nutrition will be reviewed.

#### Carbohydrate Metabolism

**Carbohydrate Digestion.**—Digestion of carbohydrate foods begins under the influence of salivary secretions. The salivary amylolytic enzyme, ptyalin, breaks down some of the ingested starches into simpler polysaccharides (dextrins) and splits these further to form maltose, a disaccharide composed of two molecules of glucose. Most of the salivary digestion takes place in the stomach after the food has been swallowed, provided that the meal is large enough to prevent immediate access of acid gastric juice to the carbohydrates, which are being hydrolyzed in the almost neutral salivary medium. No further carbohydrate digestion occurs under the influence of gastric juice, except that the soluble carbohydrates go into solution and the insoluble carbohydrates (starches) are broken up into small particles. The acid chyme, having the consistency of a thick cream soup, is then passed to the duodenum in small quantities at intervals.

The acidity of the chyme is reduced in the duodenum, where pancreatic secretions and the *succus entericus*, or juice secreted by the mucosal glands of the small intestine, are added. Both of these liquids are alkaline in reaction and both contain enzymes for carbohydrate digestion. The pancreatic amylase (diastase) is much more powerful than ptyalin and completes in a very short time the conversion of starches and other higher polysaccharides into maltose. The *succus entericus* contains enzymes (maltase, sucrase, lactase) which act specifically upon the individual disaccharides, converting them into their component monosaccharides. Maltose, the chief end product of starch digestion, is hydrolyzed completely to glucose, while sucrose is broken down into its constituent molecules of glucose and fructose. The monosaccharides then pass through the mucosa of the small intestine and are absorbed into the capillaries leading to the portal system.

**Carbohydrate Metabolism.**—Glucose (dextrose) is the chief source of carbohydrate energy in the body. It is questionable whether any of the other monosaccharides (fructose, galactose) absorbed during food digestion are utilized as such; it is more probable that they are converted into glucose in the liver through the intermediary formation of glycogen.

Glucose is a hexose (a sugar containing six carbon atoms) and exists in the body as a constant mixture of two isomeric forms, both dextrorotatory with respect to polarized light (dextrose). It is derived chiefly from carbohydrates in the diet, as described before, but may be formed in the liver from protein; for example during starvation or when the diet is deficient in carbohydrate. It is questionable whether glucose also can be formed from fat. When glucose is absorbed through the intestinal wall, it passes through the portal circulation into the liver, where part of it is converted into liver glycogen and part is oxidized. The remainder is stored in the body tissues, chiefly as muscle glycogen.

In the liver, glucose is transformed into glycogen by means of intermediate combination with phosphate groups (phosphorylation). The reaction is reversible and provides for a constant and readily available supply of glucose for hepatic metabolism, for maintenance of blood sugar levels, and, to some extent, for usage for muscular activity.

Glycogen is a polysaccharide composed of an aggregation of glucose molecules and is formed chiefly in the muscles and the liver, although small quantities are present in other tissues. Energy for muscle activity is supplied by muscle glycogen, which is broken down by successive stages through phosphorylation<sup>1</sup> into pyruvic acid. At this point, oxidation occurs and part of the pyruvic acid is transformed completely into carbon dioxide and water, the remainder being partially oxidized to form lactic acid. The lactic acid is transported by the blood stream to the liver, where it is converted into glycogen. Lactic acid is a product of muscle metabolism and is not formed from glycogen in the liver; in this organ, glycogen is transformed quantitatively into glucose, which in turn is either transferred into the blood stream or oxidized to form carbon dioxide and water.

The level of blood sugar is kept constant (normally at 80 to 110 mg. per cent) by an equilibrium maintained between its storage and release.<sup>2</sup> Absorption of sugar from the intestinal tract following digestion causes a rise in the amount of sugar in the blood. The excess is withdrawn rapidly by the liver, the muscles, and other important storage depots. Glycogen formed in the muscles is not available for any purpose except muscle energy, but glycogen formed in the liver is labile. As the amount of sugar in the blood drops below normal (between meals, fasting), liver glycogen is broken down into glucose again, and the sugar enters the blood stream until normal levels are re-established. If the amount of sugar introduced by digestion or by intravenous administration exceeds the maximum possible rate of glycogenesis, the level of sugar in the blood rises beyond the renal threshold (about 180 mg. per cent) and the excess is excreted into the urine. In the fasting subject, or when insufficient carbohydrate is ingested, the liver glycogen supply rapidly becomes depleted, and protein is metabolized by the liver to form sugar. In this process, protein is split into its constituent amino acids, which then undergo deamination and are transformed into glucose and urea. This process is kept at a minimum by maintenance of a satisfactorily high intake of carbohydrate, so that carbohydrate is said to have a "protein-sparing" action.

It is important to realize that the glycogen store in the liver is not of sufficient quantity to furnish much sugar for energy production. The average weight of the adult liver is approxi-

mately 1,500 grams, and if glycogen storage has reached its maximum of 10 per cent of the weight of the liver, there would be no more than 150 Gm. of sugar present. This amount would furnish only 600 calories of energy, even if it were all available. The chief functions of the liver glycogen store are the rapid correction of fluctuations in the blood sugar level and, no less important, the protection of the liver cell. An exogenous supply of carbohydrate therefore must be furnished at frequent intervals and in proper quantity or glucose will be formed in the liver from body proteins after the available liver glycogen store has been exhausted.

Formation, release, and storage of glucose in the liver are influenced by insulin, which regulates the blood sugar level. Insulin, in direct proportion to the amount present in the blood, causes an increased deposition of glycogen in muscle and an increased rate of glucose oxidation. The blood sugar therefore is promptly depressed by insulin. Deposition of glycogen and production of glucose<sup>3</sup> in the liver, as, for example, from protein, are both inhibited by insulin. When insulin is present only in physiologically normal amounts, the transient hyperglycemia occurring after carbohydrate ingestion results in glycogen deposition in the liver. When insulin is present in excessive amounts, as following insulin overdosage or in hyperinsulinism, the hyperglycemia following carbohydrate ingestion is of shorter duration, less hepatic glycogen is formed, and varying degrees of hypoglycemia may ensue. Under the influence of insulin, metabolic oxidation of both fat and protein is depressed as the metabolism of glucose is increased.

An interesting property of insulin is its effect on gastric peristalsis. Administration of 5 to 10 units of insulin to the normal subject an hour before meal time will cause definite hunger contractions of the stomach and increased appetite, possibly as a result of slight depression of the blood sugar level. Clinical use of insulin for this purpose in the debilitated nondiabetic patient will prove helpful sometimes in inducing the patient to take a larger diet willingly.

### Fat Metabolism

**Fat Digestion.**—No digestive alteration of fat takes place in the mouth under the influence of saliva, and little or none occurs in the stomach. There is a lipase (fat-splitting enzyme) in

the gastric juice, but it is weak and has little effect, particularly in the gastric or acid phase of digestion. The only important change undergone by fat in the stomach is partial emulsification in the chyme.

Fat digestion takes place in the small intestine under the influence of lipase, secreted chiefly by the pancreas but also present in the intestinal juices. The action of lipase consists of hydrolysis of the fat molecules into their component parts, one molecule of glycerine to three molecules of fatty acid. In the alkaline intestinal digestive medium, a part of the fatty acid thus formed combines with sodium to form soaps (sodium salts of fatty acids). These substances, by producing a reduction in surface tension, cause the still undigested fat particles to break up into smaller globules, increasing the area exposed to the action of lipase and hastening lipolysis.

Bile, secreted by the liver and entering the duodenum by way of the common bile duct, exerts a profound influence on fat digestion even though it contains no fat-splitting enzymes. Pancreatic lipase, the most important of the lipolytic digestive enzymes, is activated by the bile salts (sodium glycocholate and sodium taurocholate). Of equal importance is the reduction of surface tension effected by the bile salts, which results in emulsification of the fat particles into tiny droplets, increasing the surface area exposed to action of the digestive enzymes. A similar action is produced by the soaps formed during hydrolysis of fat, but to a much smaller degree. Fat digestion, however, may proceed to a considerable degree in the absence of bile, although the resulting products of digestion will not be absorbed to any extent.

Following digestion, or hydrolysis, by the lipolytic enzymes, fatty acids are absorbed through the intestinal epithelium in the form of an unstable molecular complex with bile salts. Immediately following absorption, the complex breaks down into its original constituents, and the fatty acid molecules reunite with glycerine molecules, also absorbed from the lumen of the intestinal tract, to form molecules of fat. The resynthesized fat is then transported to the lymphatics of the intestinal wall, down the mesenteric lymph channels, and into the thoracic duct.

**Fat Metabolism.**—The simplest of the body fats are the triglycerides, in which one molecule of glycerine is combined with three molecules of fatty acid. Fat may differ in type and properties according to the particular fatty acids which enter into its composition. It occurs stored in "fat cells" or as fatty tissue everywhere in the body except in the brain. The amount of fat present in fat depots, as, for example, in the subcutaneous tissues and in the omentum, depends to a great extent on the balance between dietary intake and energy output. Fat of this type serves chiefly as a source of energy, supplying 9.3 calories per gram, and is of particular value because it is stored in large quantities in the body, providing a large and readily available reserve of calorigenic material. Body fat is formed not only from fats ingested as such, but also from dietary carbohydrates. Protein is not transformed directly into fat, but if protein is ingested in excess of physiologic requirements, it may be altered in the liver to form carbohydrate (glucose), which is then available to form fat, with excretion of the excess nitrogen in the urine as urea.

The lipoids, or fatlike substances, of most general physiologic interest are the phospholipids, which are probably directly concerned in the intermediary metabolism of fat in the body. Lecithin and cephalin, two of the most important phospholipids, are similar in chemical structure to the fats, one fatty acid group being replaced by a phosphoric acid-choline complex in the case of lecithin and one group by an amino-ethanol complex in the case of cephalin. These substances are found in almost all the cells and tissues of the body.

The liver is intimately concerned with fat metabolism, just as it is with carbohydrate and protein metabolism. Prolonged feeding of an inadequate diet or inability to take food for even a relatively short period of time may result in the reduction of glycogen and the deposition of an excessive and abnormal amount of fat in the liver. Accumulation of fat globules in the hepatic cells increases the susceptibility of the liver to damage (for example, from relative anoxia during and after operation or from relatively toxic drugs and anesthetics). The metabolic efficiency of the liver is profoundly depressed and the liver glycogen store is reduced, both because of the impairment of carbohydrate metabolism and because of the space occupied by the fat and consequently unavailable for glycogen storage. Apparently



glycogen is necessary not only as a source of labile carbohydrate, but also as a protection for the liver cells against toxic agents.

Impaired liver function will accordingly result from increased fat deposition in the liver cells and decreased glycogen storage. Any illness which causes restriction in the quantity or quality of food ingested, or which results in a chronic loss of weight or in debility, or which produces a direct deleterious effect on the liver will result in depressed liver function either early or late in the course of the disease. A necessary phase of treatment in a patient so affected, especially if a surgical operation is contemplated, is restoration of proper liver function by decreasing the fat content of the liver and increasing the glycogen store. This may be accomplished, as Ravdin and associates<sup>4</sup> have suggested, by the feeding of a high protein, high carbohydrate, low fat diet, with supplementary administration of vitamin B<sub>1</sub> (thiamine chloride). Recent advances have made it possible to give such a diet intravenously if the patient is unable to take food by mouth.

Accumulation of excess fat in the hepatic cells may result from causes other than starvation, debilitating disease, or chronic infections. Patients with conditions causing alterations in bodily metabolism, such as diabetes and chronic pancreatitis, may develop fatty liver. The same condition may appear to a lesser degree during the latter months of pregnancy. Even more commonly, excess fat deposition in the liver may be due to habitual ingestion of a diet containing an excessive proportion of fat or deficient in certain protective factors. These protective substances, which inhibit deposition of fat in the liver cells and encourage its removal or mobilization when present, are called *lipotropic substances*.

Lipotropic factors are present in normal body tissues and are found in the average diet. *Choline*, a component of lecithin and other phospholipids, is also a constituent of bile, occurring in combination as glycocholic acid and taurocholic acid. It is of considerable importance in fat digestion and fat transport and appears to exert a protective (lipotropic) effect on the liver, inhibiting excess fat deposition and encouraging mobilization of fat from the liver when present. Loss of bile from a biliary fistula therefore is likely to interfere not only with fat digestion and absorption, but also with normal hepatic metabolism; patients with biliary tract fistulas consequently require oral administra-

tion of bile salts. *Methionine*, an essential amino acid, has a lipotropic effect, possibly because it takes part in the synthesis of choline by the body. *Lecithin* (present in egg yolk and lean meat) also is lipotropic because of its choline content. *Inositol*, recently isolated as part of the vitamin B complex, exerts a lipotropic effect. Various proteins, such as *casein*, have been found to possess the same protective effect on hepatic metabolism, possibly because of their methionine content. Finally, *pancreas* has been shown both experimentally and clinically to have the property, when ingested as a food, of removing fatty deposits from the liver. Whether this is due entirely to its content of known lipotropic substances (choline, methionine, inositol) or partly also to the presence of a lipotropic hormone (*lipocaine*) has not been finally decided. Practically, however, the administration of choline and methionine may prove to be of advantage in patients with liver damage due to disease or relative starvation. Since most of the work on lipotropic factors such as methionine and choline has been done on experimental animals up to the present time, controlled clinical studies will be necessary before the findings can be applied<sup>5</sup> to the clinical care of patients with hepatic damage.

There are also substances (for example, cholesterol) which exert an opposite or antilipotropic effect and encourage the deposition of fat in the liver. Ingestion of a high fat diet or of a relatively large proportion of foods containing cholesterol therefore may result in increased deposition of fat in the liver. Patients with conditions in which the cholesterol metabolism is disturbed (diabetes, hypothyroidism, pregnancy) may show the same hepatic changes.

Fat is metabolized in the body to produce energy, both the glycerol and the fatty acid components being oxidized completely to form carbon dioxide and water. Ketone bodies are formed as an intermediary stage in the oxidation process<sup>6</sup> and are metabolized in the body tissues, where the final stages of oxidation occur. Formation of ketone bodies from fat occurs chiefly in the liver, irrespective of carbohydrate metabolism. Normally a balance is maintained between the relative quantities of fat and carbohydrate metabolized, and ketosis does not occur. When carbohydrate intake is decreased or when glycogen is lessened and liver fat deposits are increased, as in starvation, chronic debilitat-

ing disease, severe infections, or diabetes, fat metabolism is proportionately increased and ketone bodies appear in appreciable quantities. If ketones are formed in excessive amounts, acidosis may develop, with depression of the alkali reserve and excretion of ketone bodies in the urine. In the diabetic patient such a condition may develop into severe acidosis with coma unless he is treated by the administration of readily utilizable carbohydrate together with insulin to stimulate preferential carbohydrate utilization.

### Protein Metabolism

Protein, the chief and indispensable constituent of all living cells and protoplasm, is of particular importance in the body economy. Muscle and gland tissues are almost entirely protein in composition; blood cells, enzymes, antibodies, and hormones are protein in nature; and the osmotic relations of the vascular system are largely dependent upon the proteins of the circulating plasma. Proteins are necessary for growth and for replacement of body tissue damaged either to a normal or expected extent by physiologic activity or to a more severe degree by illness or trauma. Dietary proteins consequently are even more necessary for maintenance of bodily health and strength than as a source of energy.

The protein molecule is a large and complex structure of high molecular weight composed of many amino acid units linked together. The large size of the protein molecule (proteins vary in molecular weight from 35,000 to more than 5,000,000) and the complexity of the molecular structure are responsible for many of the physical properties exhibited by the protein, such as the osmotic pressure it exerts and the degree of viscosity it imparts to a solution. Each protein, characteristic of a specific tissue throughout the body, has its own individual chemical structure, determined by the proportion of the various amino acids and other groups (for example, carbohydrates, nucleic acid, phosphoric acid) which may be attached. Certain proteins are type specific; the plasma globulin of the human being differs from that of the horse, so that animal plasma or serum may not be used directly in the human being to replace a deficit. Foreign protein or sensitivity reactions may be evoked for example following administration of antitoxic sera in an individual who has pre-

viously received an injection of serum from the same animal species.

**Amino Acids.**—The constituent units of proteins are the amino acids, each varying in chemical composition but each possessing a carboxyl (acid) group and an amino (basic) radical. Proteins are formed by interlinking of amino acids through union of the carboxyl group of one with the amino group of another (peptide linkage—Fig. 6). Grouping of a small number of amino acid units produces intermediate products known as polypeptides. More complex unions of these structures produce peptides and protein molecules. Conversely, splitting of proteins occurs by hydrolysis, the peptide linkage of each unit being separated by the introduction of a molecule of water.

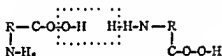


Fig 6—Peptide linkage Union of amino acid groups occurs between the carboxyl group of one and the amino group of another, eliminating a molecule of water. Hydrolysis is the reverse of the above process.

There are at least twenty-one amino acids normally utilized in the formation of body protein, although different proteins vary in their percentage composition. Of these amino acids, eleven can be synthesized by the body from other amino acids and from nitrogenous foods, while ten cannot be made in sufficient amounts and therefore must be supplied in the food in satisfactory quantities. The amino acids of which practically all proteins are composed are as follows:

ESSENTIAL	NONESSENTIAL
Lysine	Glycine
Tryptophan	Alanine
Histidine	Serine
Phenylalanine	Norleucine
Leucine	Aspartic acid
Isoleucine	Glutamic acid
Threonine	Hydroxyglutamic acid
Methionine	Proline
Valine	Hydroxyproline
Arginine	Tyrosine
	Cystine

Deficiency in the diet of even a single one of the essential amino acids will prevent growth, maintenance of nitrogen balance, repair of normal tissue damage, or replacement of protein loss. Proteins containing all the essential amino acids in satisfactory quantities (meats, eggs, milk, etc.) are known as complete proteins, while those lacking any one of them are called incomplete proteins (certain vegetable proteins). Various incomplete proteins may be used in the diet to supplement each other, since one may contain an amino acid that others lack. In this way, a complete protein diet may be obtained through a proper combination of different incomplete proteins.

For ordinary purposes an average daily dietary protein intake of 1 Gm. per kilogram body weight is sufficient, although health can be maintained on less than this quantity if the proteins are of high biologic value. In such a case, sufficient energy-producing foods must be supplied so that the protein component of the diet is utilized entirely to satisfy the nitrogen replacement requirements of the body. Excess protein in the diet is used as a source of energy, supplying 4 calories per gram.

**Protein Digestion.**—Digestion of protein foods begins in the stomach, where the proteins are dissolved by the acid gastric juice. Splitting of the complex protein molecule into simpler polypeptides known as proteoses and peptones occurs by hydrolysis under the influence of the gastric enzyme pepsin. Most of the ingested protein therefore reaches the duodenum in solution in the chyme and is next subjected to the action of the pancreatic proteolytic enzymes. Duodenal digestion takes place in an alkaline medium.

Of the pancreatic protein-splitting enzymes, trypsin is the most important. It is secreted by the pancreatic alveolar cells as trypsinogen and is activated in the duodenum by enterokinase, an enzyme present in the intestinal juice. Although the food proteins are carried into the duodenum chiefly in a partially digested state, any protein remaining unaffected by the gastric juice will be digested by the tryptic ferments. Essentially, the proteoses and peptones in the chyme are hydrolyzed further by trypsin to form simple peptides and polypeptides, which contain only small numbers of constituent amino acids. Final hydrolysis or digestion of peptides into amino acids is

effected during passage through the small intestine by peptidases (erepsin) secreted by the intestinal glands.

**Protein Metabolism.**—The amino acids are absorbed through the small intestine and are carried to the liver by the portal blood stream. Some of them are required in other parts of the body for repair, replacement, or growth of cellular tissues or for formation of necessary protein secretions (hormones, enzymes). These amino acids pass through the liver unchanged and reach their destination through the vascular system. Amino acids which are not needed or cannot be utilized as such are broken down chiefly in the liver, the first step being the splitting off of the amino group by oxidation to form urea (deamination). The remaining radical is either oxidized completely or transformed into glucose for immediate or future use. When one or more of the essential amino acids are lacking in the dietary protein, the body is unable to utilize any of the component amino acids for growth or repair. Under these circumstances all the amino acids are deaminated and the nitrogen is lost in the urine. On the other hand, if the essential amino acids are all present in sufficient quantity in the diet and the nonessential ones relatively deficient, the lacking nonessential amino acids may be synthesized by the body. One of the most interesting views of protein metabolism to be advanced in recent years is that the body proteins are not fixed but are in a state of constant interchange,<sup>7</sup> with the nitrogenous constituents of the various cells and organs exchanging back and forth with each other and with the plasma proteins in an unceasing flow, whether or not dietary amino acids are added. It is probable that a readily available store of protein is present in the body tissues, not as an integral component of the cells or plasma but in a more labile form—a protein reserve that can be drawn upon for a short time as needed during illness, starvation, or increased metabolism.

Normally, a certain amount of body protein is broken up or metabolized by physiologic activity. Even if an individual receives no food, the daily excretion of nitrogen in the urine and feces amounts to several grams. Protein foods are utilized to replace the worn or damaged body tissues, the necessary amount of nitrogen in the form of amino acids being retained and the remainder or excess of the food amino acids being transformed

into glucose or fat or being oxidized for energy. The excess nitrogen is excreted, chiefly in the urine as urea. The ratio between the nitrogen excreted and the nitrogen ingested is called the *nitrogen balance*. Obviously, when the nitrogen intake is less than the amount excreted, the nitrogen balance is negative and the body tissues are not being maintained in a healthy state. When the nitrogen intake is greater than the output, the individual is retaining nitrogen and lost body protein is being replaced. The nitrogen balance is therefore positive. It is possible, however, for the nitrogen intake to be relatively high and yet be almost entirely excreted; even a starving individual cannot utilize incomplete proteins to replace tissue protein. Food proteins which resemble the body proteins most closely with respect to amino acid composition (milk, eggs, meat) have the highest biologic value and are the most satisfactory for replacing tissue losses. Also, the quantity of such proteins necessary to maintain a positive nitrogen balance is smaller than the amount of proteins of lower biologic value needed (for example, vegetable proteins).

**Plasma Proteins.**—The concentration of the plasma proteins amounts to approximately 6.5 to 8.0 Gm. per 100 c.c. of plasma, with an average of 7.2 Gm. per cent. The chief proteins of the plasma are serum albumin (average concentration, 4.5 Gm. per cent), serum globulin (average concentration, 2.6 Gm. per cent), and fibrinogen (approximately 0.2 Gm. per cent). Fibrinogen is synthesized in the liver; albumin and part of the globulin also are formed there, although there is evidence that serum gamma globulin, at least, has an extrahepatic origin.<sup>8</sup>

One of the chief functions of plasma proteins is maintenance of the osmotic pressure of the blood, normally 25 to 30 mm. of mercury. Proteins are particularly effective in this respect because the large size of the protein molecule interferes with its passage across the cell membranes, and it is consequently retained in the vascular system. All the plasma proteins exert some osmotic effect, although albumin is the most important. Approximately 85 per cent of the osmotic pressure of the plasma is due to the albumin,<sup>9</sup> which is present in excess of globulin in the ratio of about 1.5 to 1. The plasma proteins also help stabilize blood pressure by contributing to the viscosity of the blood and

aid in regulation of the acid-base balance by acting as weak acids in combination with alkali. The serum globulin is chiefly responsible for the transport in the vascular system of immune substances, antibodies, and agglutinins. The plasma proteins, particularly albumin, also act to some extent as a ready source of available protein in the fasting patient. Fibrinogen is directly concerned with the formation of fibrin in the clotting process. Removal of fibrinogen from the plasma removes its power to form a clot, and the defibrinated plasma is called *serum*.

Conditions in which the plasma proteins are increased in amount are of less direct clinical surgical interest than those in which they are decreased. Loss of body protein, deficient protein intake, or impaired protein digestion and absorption will soon produce a negative nitrogen balance. Further loss of body protein, loss of weight, and a resultant drop in plasma protein will develop. Because the tissue proteins are in a balanced equilibrium, a decrease in one protein depot is always reflected to some extent in others. The hypoproteinemia is thus related directly to the loss of protein from all the body tissues; it has been estimated that for each gram of plasma protein deficiency, there is a concomitant loss of approximately 30 Gm. of tissue proteins.<sup>10</sup> For this reason full replacement of depressed plasma proteins cannot be achieved simply by the administration of several plasma or blood transfusions.

Hypoproteinemia may be masked by fluid loss; chronically ill patients may show a normal plasma protein concentration at the time of admission to the hospital. Dehydration develops in such patients as a result of plasma protein deficiency in order to maintain relative plasma protein concentration and plasma osmotic pressure within the normal range. Correction of the dehydration by administration simply of fluids and salt will result in dilution of the plasma and tissue fluids, with reduction in vascular osmotic pressure and possible development of edema, latent or clinical.<sup>11</sup> Depression of the serum proteins to a level of 5 Gm. per cent or less usually will be followed by edema. Because of lowered intravascular osmotic tension, fluids and salt will pass readily out of the blood stream into the tissues, with waterlogging proportionate in degree to the lowering of osmotic pressure. In these chronically ill patients administration of



proper quantities of fluid, electrolytes, and carbohydrates must be accompanied by restoration of lost protein.

**Protein Loss.**—*Acute protein deficiency* often results from conditions causing sudden loss of large quantities of protein. Severe hemorrhage, shock, extensive burns, serious trauma, or acute intestinal obstruction all exhibit marked tissue and plasma protein loss as part of the clinical picture. The deficiency is aggravated by the fact that patients with these types of illnesses are unable to take protein foods by mouth except in very small quantities.

*Chronic protein deficiency* develops more slowly and may result from low protein intake or absorption, from excessive loss of protein-containing fluid, or from hypermetabolism. Disease of the gastrointestinal tract, particularly if accompanied by vomiting or diarrhea, decreases the protein intake and interferes with protein absorption. Cachectic disease due to any cause reduces the appetite and consequently reduces the protein available for tissue metabolism. Patients with conditions characterized by the production of purulent exudates<sup>12</sup> (osteomyelitis, empyema) or transudates (cirrhosis) require increased intake of protein food to replace the body protein lost by drainage. Trauma of any type, including surgical operation<sup>13</sup> and anesthesia, or hypermetabolic disease such as toxic goiter will increase nitrogen catabolism and loss of tissue protein.

Following a surgical operation, a patient may lose one to two pounds of weight each day, particularly if an untoward complication develops. Prolonged convalescence then ensues and full recovery does not occur until the patient has absorbed sufficient nitrogenous food to repair his losses of muscle and tissue protein. It is worth while to realize that postoperative or posttraumatic weight loss is not simply a reflection of lost body water and body fat but represents to a considerable degree a loss of body protein that must be replaced. When the patient is unable to eat satisfactorily because of gastrointestinal tract disease or is unable to manufacture body protein properly because of hepatic damage, attainment of a positive nitrogen balance presents a serious problem.

Extent of protein loss may be approximated by calculation from the serum protein changes. Elman and associates<sup>10</sup> state

that each gram that the serum albumin is decreased reflects a loss of about 30 Gm. of tissue protein. For example, a decrease of 1.0 Gm. per cent in serum albumin in an adult would amount to a loss of 1 Gm. from each 100 c.c. of the total plasma volume (2,500 to 3,000 c.c.), or a total of approximately 25 to 30 grams. If each gram reflects a loss of 30 Gm. of tissue protein, the deficit in body protein would amount to from 750 to 900 grams. For proper replacement, at least this amount of fully available protein must be given to and absorbed by the patient in addition to the amount required to maintain a normal daily nitrogen balance. Since the average daily dietary protein intake of 60 to 80 Gm. is sufficient only for maintenance of normal nitrogen balance, the problem involved in supplying so much additional protein is obviously serious.

It should be noted, however, that these ratios are approximations and that the wide variations in total plasma volume that occur in acute or chronic illness must be taken into account. Loss of body protein first causes a decrease in the labile protein stores and then a wasting or catabolism of the structural tissue proteins. The loss of tissue protein is evidenced not only by a rise in urinary nitrogen excretion, but also by a fall in serum protein concentration. Serum albumin is more readily utilized as an endogenous source of food protein than is serum globulin, and its smaller molecular structure renders it more likely to be lost from the blood stream by transudation across the capillary wall. As a result of the disproportionate fall in serum albumin, the albumin/globulin ratio, normally 3.2, decreases and may even be reversed.

As previously stated, loss of plasma proteins during starvation or malnutrition is accompanied by a partially compensating decrease in total blood volume (dehydration). Under such circumstances the total plasma proteins may be deceptively close to normal. Determination of the individual plasma proteins in such a case will reveal a decrease in serum albumin concentration, while the serum globulin may be actually higher than normal. In general, however, alterations in the albumin/globulin ratio are dependent upon so many widely divergent factors that little diagnostic significance<sup>14</sup> can be attached to this value.

Correction of the dehydration, to the point at which urinary excretion totals from 1,000 to 1,500 c. c. each day, will cause a reduction in plasma protein concentration to a level more nearly approximating the true value. It is at this point that estimation of the total protein loss may be made more accurately by calculation based on the plasma protein deficit. However, it is worth noting that there are wide variations in the total blood volume in sickness and in health and that even though fluid is supplied until urinary excretion is normal, the total blood volume of a chronic invalid is by no means the same as the total blood volume of the same individual in his previous state of perfect health.<sup>42</sup> Quantitative estimations of total protein loss computed from plasma protein deficits therefore are only rough approximations at best unless alterations in the total plasma volume<sup>43</sup> are taken into account. Such approximations, however, are of value in emphasizing the extent of tissue protein loss that is evidenced by a relatively small decrease in plasma protein concentration.

**Effects of Protein Deficiency.**—Susceptibility to shock is increased. Hypoproteinemic patients show little reserve and react poorly during and after operation. As a rule, surgical procedures are not performed upon such individuals unless the operation is either a very minor one or a dire emergency. In the latter case, transfusion of blood or plasma in large quantities is begun at once and is continued until enough has been given, preferably before operation, to maintain the blood pressure at a satisfactory level. Close watching is necessary for several days after operation.

When the depleted fluid and electrolytes in the hypoproteinemic patient are restored to normal, transudation of water and salt into the tissues occurs. Edema then develops and will interfere with normal tissue physiology and will delay wound healing. For instance, following gastrointestinal anastomoses in such patients edema is likely to develop at the stoma<sup>44</sup> and interfere with normal peristalsis. Partial or complete obstruction with its accompanying problems may result. The same type of nutritional edema may occur around the pylorus in the presence of a chronic lesion that has interfered with food intake, and obstruction may result (p. 609).

Recovery from extensive wounds, severe burns, or shock is impeded by protein deficiency. Regeneration of lost or destroyed tissue and plasma proteins cannot occur unless an excess of satisfactory protein or amino acid food is supplied. The relation of protein intake to convalescence and recovery of full health following operation has been accorded its full importance only recently.

Visceral function, gastrointestinal tract peristalsis, normal enzymic digestion of food, and circulatory efficiency are all affected adversely by protein lack. In chronic deficiency states, the fat content of the liver is increased, with a corresponding drop in hepatic functional capacity<sup>1</sup> and a decrease in the rate of synthesis of plasma proteins and even of prothrombin.<sup>14</sup>

Healing of wounds, whether traumatic or surgical, is delayed by hypoproteinemia.<sup>15</sup> This fact has been demonstrated unequivocally both clinically and in the laboratory. It holds true for ulcerated lesions as well. Mulholland<sup>20</sup> and co-workers have shown that decubitus ulcers may be healed in many patients by administration of relatively large amounts of amino acids and that patients with chronic leg ulcers respond almost equally well. Co Tui<sup>21</sup> and associates have reported considerable success in the nonoperative treatment of patients with peptic ulcers by the administration of protein hydrolysates orally (p. 606), with fairly prompt healing in a large percentage.

Resistance to infection is lowered<sup>22</sup> in protein-starved patients, whether because of the impaired visceral function, or the depressed antibody and leucocyte response, or the decreased protein available for local inflammatory reaction. Pneumonia, atelectasis, thrombophlebitis, intestinal obstruction, and most of the other serious postoperative problems also are more likely to develop in these debilitated subjects. The protein requirement is raised considerably above normal by a surgical procedure alone, and an associated or subsequent complication increases the need still more.

With every instance of protein deficiency due to a restriction in diet or a defect in absorption, there is almost always an associated multiple vitamin deficiency and often a chronic secondary anemia. Replacement of the necessary lacking elements is requisite before operation and is continued during the period of convalescence.

## Protein Replacement

**Acute Protein Deficiency.**—Loss of body protein following severe trauma with actual or impending shock, extensive burns, or acute hemorrhage requires emergency treatment. Blood lost is restored promptly by transfusion of matched blood, and lost plasma is restored by transfusion of human plasma or concentrated serum albumin. Unusually large quantities are required occasionally; for example, in extensive burns as much as 3,000 to 4,000 c.c. of plasma may be given intravenously each day for the first two days following the injury. Administration of plasma on this scale must be regulated by frequent plasma protein, hematocrit, and hemoglobin determinations, since overdosage may contribute to development of pulmonary edema. Volume of urinary output also may be used as a check on adequacy of body fluid replacement. Patients suffering from severe burns or traumatic shock may exhibit oliguria during the first two days after injury, perhaps from insufficiency of circulating blood volume as well as from decreased blood pressure. Proper replacement of lost blood or plasma will be followed by a urinary output of satisfactory volume, with a specific gravity in the middle range.

Theoretically, plasma loss is treated best by plasma replacement and blood loss by blood transfusion. Practically, however, blood transfusions produce a more prompt and sustained restoration of blood pressure in shock or impending shock due to any cause, including burns. Plasma is somewhat safer in an acute emergency, since it may be given in relatively large amounts in continued dosage without cross matching. The best plan therefore is administration of plasma until compatible blood can be obtained and then transfusion of 1,000 to 1,500 c.c. of blood as rapidly as necessary, with subsequent use of blood or plasma as indicated.

### Chronic Protein Deficiency.—

Chronic deficiency states develop more slowly and to a more profound degree than protein lack secondary to acute conditions. Chronic hypoproteinemia cannot be corrected completely by plasma or blood transfusions, which supply only a small amount of protein. Moreover, both hemoglobin and albumin<sup>22</sup> are relatively deficient in at least two of the essential amino acids. The

protein content of plasma averages about 7.0 Gm. per 100 c.c. so that a liter of plasma will supply only 70 grams. In deficiency states, when each gram of plasma protein deficiency reflects a loss of perhaps 30 Gm. of tissue protein, it is evident that the quantities of plasma required to supply enough protein would be too large as well as too expensive to be practical for nutritional therapy. On the other hand, chronic hypoproteinemic states are always accompanied by dehydration, reduction of total blood volume, and decrease in total red cell mass. The first step in correction of this condition therefore is to administer whole blood transfusions until the blood volume has been restored to normal.<sup>22</sup>

The ideal method of replacing lost tissue protein is to supply a diet containing from 150 to 250 Gm. of biologically complete protein each day in addition to the proper amounts of carbohydrate and fat to supply adequate calories. However, it is difficult for even a healthy person to eat this much protein food for more than a day or two at a time, and an invalid cannot be expected to do so, particularly if gastrointestinal tract disease is present. It is necessary therefore to supplement the dietary protein with protein in other forms.

**Protein Substitutes.**—During the past few years, the combined research of a great many investigators has produced methods of administering proteins parenterally<sup>24</sup> in the form of their constituent units, the simple amino acids. Continuing work in this field holds promise of supplying the answers to many problems in surgical physiology, nutrition, and healing that at present are still treated more or less empirically.

Amino acids are the building units or structural components of proteins. For replacement of body proteins, all ten of the essential amino acids, in addition to supplementary quantities of the nonessential ones, must be supplied in adequate amounts. Lack of any one of the essential amino acids prevents the use of any of the others for building protein, no matter how large the quantity supplied. Pure amino acids (crystalline) in proper amounts and proportions have been given to patients and were found to be fairly satisfactory in achieving positive nitrogen balance. At the present time this method of administering protein therapeutically is not practical because of the expense.

A mixture of amino acids can be produced by hydrolysis of certain proteins (for example, casein, which is a protein of high biologic value). If pork pancreas is used as the hydrolyzing agent (enzymic hydrolysis), the pancreatic enzymes split both the casein and the pancreatic proteins into their component amino acids, a portion of which remain linked together as simple peptides. Enzymic hydrolysates of this type are highly satisfactory as sources of protein and can be given orally, intravenously, or by stomach tube. Casein also may be split into its component amino acids by acid hydrolysis. However, acid hydrolysis destroys most of the tryptophan, and this essential amino acid therefore must be added to the hydrolysate. All the amino acid nitrogen in these hydrolysates is available for synthesis of protein in the body.

There is evidence that feeding of the complete protein either by mouth or by tube is more effective than administration of protein hydrolysate by any route. Madden<sup>25</sup> and co-workers maintain that complete proteins are more effective clinically than amino acid mixtures, and Womack and Rose<sup>26</sup> have shown that this is true in experimental animals. Other studies<sup>27</sup> have demonstrated that growth in laboratory animals fed on amino acid mixtures is stimulated by the addition of small amounts of casein to the diet. It is suggested<sup>28</sup> that there is a growth-stimulating substance ("strepogenin") present in certain proteins, such as casein, hemoglobin, and trypsinogen, but not present in others, such as egg albumin and gelatin, which do not show similar growth-stimulating effect when added to the diet in test animals. The substance is thought to be a peptide that is broken down during the process of either acid or enzymic hydrolysis of, for example, casein. Eventual isolation of this factor may permit its addition to protein hydrolysates to make them as effective as complete proteins for nutrition and growth.

**Oral Protein Replacement.**—*Correction of protein deficiency* by high protein diet is the simplest and best method when it can be used. The average standard hospital diet for all surgical patients should be high in protein (at least 1.5 Gm. per kilogram of body weight) and should furnish at least 2,500 calories a day. A relatively low fat and high carbohydrate pro-

portion is preferable. An increase in the amount of protein in the diet is best achieved by addition of proteins of high biologic value, such as extra milk, meat, fish, eggs, cheese, peas, and beans. Large amounts of these foods cannot be eaten regularly over a long period of time, so that only relatively small increases in dietary protein can be made in this manner.

Patients with *protein depletion* should receive a high protein, high carbohydrate, low fat, high vitamin, high caloric diet. Depending on the particular patient, such a diet should contain from 3,000 to 5,000 calories. If the patient becomes nauseated and unable to eat so much, a decrease in the percentage of fat in the diet may make it more acceptable and less satiating.

Experience has shown that such a diet must be ordered in specific detail. In many cases, when an order is noted on the patient's chart for a "high caloric, high vitamin, high protein, low fat, high carbohydrate" diet, the diet supplied is simply the hospital regular diet. The order should always state the amount of protein and the number of calories desired, the percentage of fat permitted (15 to 25 per cent), and whether supplementary between-meal feedings are desired. The type of extra feedings ordered also must be stated.

Frequently, even if the patient is properly served, the meals are not eaten. An invalid with a poor appetite will not make a sustained effort to take all his food unless someone, either a nurse or a relative, is present at mealtimes to encourage him to do so. Furthermore, even if a desire to cooperate is present, it may be difficult to eat three large meals every day. The trays should be made attractive in appearance, the patient's likes and dislikes consulted, and, above all, the food should be hot, palatable, and fresh. Meals that are refused or only partly consumed or food that is lost by vomiting or is not absorbed because of diarrhea are noted so that replacement may be made by other means of protein administration.

Supplementary feedings are given between meals three to five times a day. These can be devised by the hospital dietitian and usually contain milk with added cream, skim milk powder, casein or lactalbumin, eggs, lactose, Dextrimaltose, corn syrup, chocolate, vitamin concentrates, and water. These may be mixed in any composition and any proportion desired, with or without the addition of protein hydrolysates. Such mixtures



can be made up to supply from 1,000 to 2,000 calories per liter and, even without added amino acids, up to 100 Gm. of protein per liter.

Amino acid preparations or protein hydrolysates will supply protein nitrogen in a form that can be rapidly absorbed from the gastrointestinal tract without need for digestion. This type of feeding is indicated chiefly for patients with diseases or affections of the gastrointestinal tract which interfere with protein digestion. In all other patients, milk protein concentrates (for example, Casec) or even skim milk powder are just as satisfactory sources of protein nitrogen as are amino acids or protein hydrolysates but require digestion before they can be absorbed and utilized. Skim milk powder, which is very inexpensive and contains approximately 35 per cent of biologically effective protein, can be given alone as a supplementary feeding in quantities of 1 to 2 ounces mixed with water every three hours during the day. The mixture tastes almost the same as ordinary milk and in the suggested dosage will supply from 90 to 150 Gm. of protein each day. Patients do not object to this type of feeding and take it readily, especially when sugar and vanilla are added.

Pure amino acid mixtures and protein hydrolysates have an unpleasant taste. Because of their unappetizing flavor, the patient is likely to offer some resistance to taking them if they are presented as foods, while if they are offered simply as medications, there will be a great deal less opposition. Most people more or less expect medicines to have an objectionable taste but will balk at food products that do not appeal to the senses. Protein hydrolysates are best given simply as a 10 to 30 per cent solution in water or glucose solution in amounts of 100 to 200 c.c. every two to four hours during the day. The taste is minimized if the patient swallows the dose quickly and immediately drinks a little grapefruit juice or lemonade. The effort required to take the protein hydrolysate regularly is well worth while, because each dose of 20 to 30 Gm. of pure hydrolysate taken will furnish almost 20 to 30 Gm. of readily assimilable pure protein. By this means alone, from 100 to 150 Gm. of protein can be given daily in addition to the protein in the diet. Proprietary preparations of mixed composition are not necessarily the most effective; if the patient can digest protein, milk protein concentrate or skim milk powder is entirely satisfactory,

while if digestion is impaired, a pure protein hydrolysate is most effective.

If the nutrient mixture is reasonably palatable, the patient can be permitted to take his own feedings. A bottle containing several hundred cubic centimeters of the nourishment can be fitted with a two-hole rubber stopper, one for an air inlet and one for a glass tube ending below the surface of the liquid. If the bottle is kept in a bowl of cracked ice, it may do for several hours without refrigeration. Varco<sup>22</sup> has suggested that a bottle of this type be placed in a bowl of ice on a stand, with a long rubber tube attached to the outlet and to the patient's pillow, being secured to the latter by a safety pin (Fig. 7). A pinch-

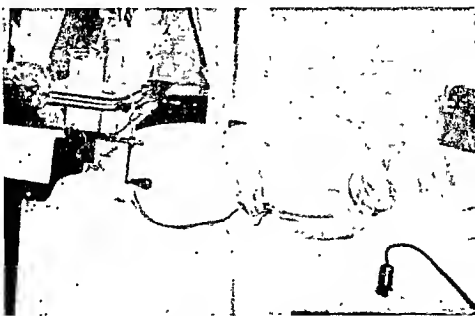


Fig 7—Sipper apparatus (From Varco *Surgery* 19: 303, 1946)

clamp is attached within reach of the patient's fingers and a mouthpiece is attached to the end of the tube, so that he may feed himself often during the day. Large amounts of nourishment can be given in this manner.

**Feedings by Tube.**—Patients who are unable to take sufficient food or supplementary feedings by mouth can be fed by stomach tube. A soft rubber tube of narrow caliber is passed

through the nose until not more than several centimeters have reached the stomach. Excess tubing in the stomach interferes with gastric peristalsis and causes anorexia and nausea. The tube may be left in place as long as necessary but is removed, cleaned, and reinserted through the other nostril every two or three days. Feedings are given with a bulb syringe. Any air that may be present in the stomach is aspirated with the syringe first and the liquid feeding then is introduced slowly. Care is taken to prevent introduction of any air with the feeding and the tube is clamped off again before the syringe is disconnected. Discomfort or distention following feedings usually is due to air in the stomach or bowel.

Formulas for tube feeding may be made up simply of protein hydrolysate with added dextrose and vitamin preparations. These are probably the best mixtures for use in the early post-operative period when digestion is most disturbed. From 150 to 250 Gm. of protein preparation, dissolved in a relatively small volume of 10 per cent dextrose solution and administered in amounts of 75 to 100 c.c. each hour or two, may be given each day. Additional protein hydrolysate solution can be given intravenously during this time if necessary. Fluids are given parenterally as required.

For nutrition of patients who are better able to digest food elements but who are unable to eat, more fully balanced formulas may be devised. These should be simple and of high nutritional value and can be made up to contain protein, fat, and carbohydrate in proper proportions, with added vitamin preparations and minerals as indicated. Skim milk powder alone, suspended in water, makes a valuable and nonsatiating mixture for tube as well as for oral feeding. Tube feedings are given every two to three hours and in many cases may be given throughout the night without disturbing the patient.

Stare and Thorn<sup>10</sup> have devised a concentrated nutritive mixture for tube feeding, supplying 120 Gm. of protein and over 3,000 calories in a volume of 1,500 c.c. (Table I). Solutions and mixtures of this type are particularly liable to bacterial decomposition. Not more than one day's supply for oral supplement or tube feeding should be made up at one time. The unused portion is kept in the refrigerator and need not be warmed before administration.

TABLE 1. FORMULA OF HIGH NUTRITIVE VALUE FOR TUBE FEEDING  
(FROM STARE AND THORN: J. A. M. A. 127: 1120, 1945.)

Total volume about 1,500 c.c. Should be made up fresh daily and kept in a closed container in refrigerator. Mixing in good mechanical mixer is necessary in preparation. Give feedings of approximately 100 c.c. conveniently spaced throughout the day and/or night. Material is most readily given with a 50 or 100 c.c. syringe through a small nasal tube, which may be left down for three to four weeks. Use alternate nostrils at weekly intervals. The mixture may be given just as it comes from the refrigerator—it is not necessary to warm it.

	CALORIES	PROTEIN (GM.)	CA (GM.)	FE (MG.)	VITAMIN A (I. U.)	THIA- MINE (MG.)	ASCORBIC ACID (MG.)	BIOTIN FLAVIN (MG.)	NIACIN (MG.)
Milk, 1 pt.	330	16.8	0.56	1.0	816	0.19	5	0.86	0.53
Cream, 1 pt. 18 to 20%	998	14.0	0.43	1.0	5,760	0.14	..	0.62	..
Raw liver* (freed of tendons), 4 oz. or 120 Gm.	158	23.0	0.01	9.8	33,000	0.38	37	3.00	17.00
Raw eggs, 4	316	25.6	0.11	5.4	1,980	0.28	..	0.74	0.12
Dried yeast, † 2 tbsp. or 20 Gm.	72	10.0	0.02	4.0	..	3.20	..	0.80	8.00
Glucose or lactose or sucrose or Karo syrup, 225 Gm. or 7½ oz.	900	5.6	0.21	..	310	0.07	1	0.35	0.15
Whole milk powder, 4 tbsp or 22 Gm.	109	35.0	..	..	..	..	..	..	..
Casain, 4 tbsp. or 30 Gm.	120	..	..	..	..	..	..	..	..
Applesauce, apple powder or pectin ‡ (4 tbsp. or 60 Gm.-applesauce)	49	0.1	....	0.1	30	..	..	..	0.02
Salt, 10 Gm.	..	..	..	..	..	..	..	..	..
Totals for foregoing	3,052	119.1	1.33	21.7	41,896	4.26	43	6.37	25.82
Orange juice, 4 oz. or 120 c.c. (give half with one of a. m. feedings and half in p. m.)	59	1.1	0.03	0.4	300	0.09	54	0.03	0.26
Complete totals	3,111	120.2	1.36	22.1	42,196	4.35	97	6.40	26.08
Salt concentration about 12 Gm.	..	..	..	..	..	..	..	..	..

\*Ground beef or pork may be alternated with liver.

†If considerable distention or diarrhea develops, substitute with equal amount of wheat or corn germ

‡This ingredient is added to prevent diarrhea and must be adjusted to the individual.

**Intravenous Protein Feeding.**—As a rule, intravenous feedings of protein hydrolysate are given only to debilitated or acutely ill patients, since most patients have sufficient reserve to withstand several days of postoperative starvation. Intravenous protein replacement therapy is of the greatest value when gastrointestinal function is so completely disturbed that feedings cannot be given in satisfactory quantities either orally or by stomach tube. Protein hydrolysates are also given by vein to supplement oral or tube feedings when an especially large amount is required, as in severe burns, extensive wounds, widespread pyogenic infections, or nutritional edema.

Protein hydrolysate solutions are given intravenously as a sterile 5 per cent solution in distilled water or in 5 per cent dextrose solution. It is unwise to use normal salt solution concomitantly, since most commercially supplied protein hydrolysates contain sodium chloride in significant amounts. The solution is administered through a 20 or 21 gauge needle at the rate of 60 to 120 drops (4 to 8 c.c.) per minute, from two to four hours being required for the introduction of 1,000 c.c. of solution. Because of the length of time required, not over 2 or, rarely, 3 liters of protein hydrolysate solution can be given in each twenty-four hour period. Since each liter of 5 per cent hydrolysate solution contains 50 Gm. of hydrolyzed protein, quantities of from 100 to 150 Gm. of biologically complete protein can be administered intravenously each day. If 5 per cent dextrose solution is used as the vehicle, the patient will also receive 100 to 150 Gm. of carbohydrate at the same time. Additional feedings of protein or of protein hydrolysate must be given by mouth or by tube as required.

In many cases, the patient himself can regulate the speed of flow through the intravenous set. Rapid intravenous administration of amino acid or protein hydrolysate solution will induce nausea and vomiting, which disappears promptly if the rate of flow is reduced. A screw clamp on the tubing within reach of the patient's free hand will permit him to adjust the flow to the optimum rate.

Because of the slowness of infusion, it is difficult in practice to administer more than 2 liters of protein hydrolysate in any one day. Elman,<sup>31</sup> who has done a great deal of valuable work on protein nutrition in surgical patients, suggests the plan presented in Table II for parenteral feeding.

TABLE II. A PROGRAM FOR DAILY PARENTERAL FEEDING (INCLUDING AMINO ACIDS)\*  
(FROM ELMAN: J. A. M. A. 123: 659, 1945.)

Initially larger doses and plasma or whole blood transfusions may be required to meet acute deficits.

	SOLUTIONS REQUIRED	ACTUAL AMOUNT OF NUTRIENTS				
		H <sub>2</sub> O (C.C.)	SALT (GM.)	GLUCOSE (GM.)	PROTEIN AS AMINO ACIDS (GM.)	CALORIES
A. No protein depletion	Protein hydrolysate 5%—glucose 5%. 1 liter; glucose 5%, 1 liter, isotonic solu- tion of sodium chloride,† 1 liter	3,000	11	100	50	600
B. Moderate protein depletion	Protein hydrolysate 5%—glucose 5%, 2 liters, isotonic solution of sodium chlo- ride,† 1 liter	3,000	13	100	100	800
C. Severe protein depletion	Protein hydrolysate 5%—glucose 5%, 3 liters	3,000	6	150	150	1,200

\*Vitamins are given separately. In certain surgical patients vitamin C is especially indicated in doses of 1 Gm. per day.

†After severe operations it may be inadvisable to inject saline solution in view of the evidence indicating the existence of a postoperative intolerance to salt (Collier, F. A., and others. Postoperative Salt Intolerance, Ann Surg 119: 513, 1911). In such cases 5 per cent glucose in water is substituted for the isotonic solution of sodium chloride.

## Summary

### Corrective Dietary Therapy.—

#### PRINCIPLES.—

1. Daily fluid requirement averages 2,500 c.c. plus any amount lost by drainage from the gastrointestinal or biliary tracts. Of this fluid intake, 1,500 c.c. is needed for heat regulation and about 1,000 c.c. for urinary excretion.

2. Daily salt requirement is not over 8 to 10 grams. This amount will be supplied by 1 liter of normal salt solution if the patient takes little or no food by mouth. More than this amount of salt rarely is necessary and sometimes may be harmful.

3. Daily dietary protein required to maintain normal or positive nitrogen balance in health is about 1.0 Gm. per kilogram of body weight.

4. Daily intake of fat is not necessary during the period of surgical treatment and convalescence

5. The carbohydrate stored in the liver (glycogen) and available for metabolic oxidation amounts to less than 100 Gm. or somewhat less than a day's dietary carbohydrate requirement. Carbohydrate therefore should be supplied every day.

6. In starvation, energy is supplied by the oxidation of body fat together with carbohydrate. If carbohydrate is not supplied, protein will be oxidized in its place. Starvation causes loss of body protein as well as of fat.

7. Administration of carbohydrate alone will spare destruction of body protein to some extent during starvation

8. Acute protein loss (shock, burns, severe trauma) requires rapid large-scale replacement (transfusions of blood and plasma) at once and sustained replacement later (high protein diet with or without extra administration of amino acid preparations).

9. Chronic protein loss may not be immediately evident in the findings of laboratory tests. Dehydration will mask moderate hypoproteinemia and anemia. Restoration of depleted water and electrolytes will cause a drop in hematocrit values and a drop in plasma protein concentration to more accurate values. Latent or even clinical edema then may result.

10. Hypoproteinemia reflects tissue protein depletion in a ratio of approximately 30 Gm. of tissue protein deficiency for each gram of total plasma protein deficiency (p. 65).

11. Deleterious effects of protein deficiency may include: lowered resistance to shock, lowered tolerance to surgical procedures, lowered resistance to infection, subnormal visceral functioning, edema of the gastrointestinal tract (especially in regions of anastomosis) and interference with peristalsis, impaired wound healing, and slow convalescence.

12. Correction of chronic protein deficiency requires transfusion of whole blood and high protein, high carbohydrate, low fat, high vitamin, high caloric diet, according to the degree of deficiency.

13. Since the normal daily dietary protein requirement in health is 1.0 Gm. per kilogram of body weight, the requirement in patients with starvation or protein depletion increases to from 2.0 to 5.0 Gm. per kilogram of body weight, according to the degree of starvation or of protein loss. A protein intake of this magnitude will amount to from 125 to 300 Gm. of protein each day.

14. Plasma, supplying only 65 to 70 Gm. of protein per liter, and requiring the drawing and processing of four blood transfusions for each liter, is unsatisfactory, too difficult to obtain, and too expensive.

15. As much protein as possible should be given by diet, supplemented with feedings of complete proteins or hydrolysate preparations by mouth or tube, or protein hydrolysate by vein to make up the total. Carbohydrates, fluids, salt, and vitamins also are given in the proper amounts. Whole proteins (for example, skim milk powder) are quite as effective as protein hydrolysates if the patient's digestion is unimpaired.

16. Requirements for certain vitamins are increased in disease.

Thiamine (vitamin B<sub>1</sub>) functions as an active coenzyme in the metabolism of carbohydrate, and the requirement for this vitamin is increased by an increase in dietary carbohydrate. The basic requirement is 0.6 mg. per 1,000 dietary calories. In starvation and malnutrition, several times this amount is given, with a minimum therapeutic dose of 10 mg. a day.



Nicotinic acid, while probably not necessary in increased amounts during the relatively short period of illness and convalescence, also is concerned with carbohydrate metabolism and might well be given. The basic daily requirement (p 210) is 10 to 20 mg. and the usual dose for patients with nutritional deficiency amounts to from 100 to 200 mg. daily.

Ascorbic acid (vitamin C) is not stored in the body in large amounts and subclinical deficiencies are common. This vitamin is concerned with connective tissue integrity and repair and is of particular importance in insuring satisfactory wound healing. Patients have been known to develop deficiency of vitamin C on a routine hospital diet during long stays in the hospital. The daily requirement in normal health is from 30 to 40 milligrams. Doses of at least 400 to 1,000 mg. a day are advised for surgical patients who exhibit nutritional deficiencies of any type or degree.

### References

1. Cori, C. F., and Cori, G. T.: Carbohydrate Metabolism, *Ann. Rev. Biochem.* 10: 151, 1941.
2. Soskin, S.: Blood Sugar: Its Origin, Regulation, and Utilization, *Physiol. Rev.* 21: 140, 1941.
3. Best, C. H., and Taylor, N. B.: *The Physiological Basis of Medical Practice*, Baltimore, 1945, Williams & Wilkins Co.
4. Ravdin, I. S., Thorogood, E., Riegel, C., Peters, R., and Rhoads, J.: The Prevention of Liver Damage and the Facilitation of Repair in the Liver by Diet, *J. A. M. A.* 121: 322, 1943.
5. Council on Pharmacy and Chemistry: The Status of Methionine in the Prevention and Treatment of Liver Injury, *J. A. M. A.* 133: 107, 1947.
6. MacKay, E. M., Wick, A. N., and Barnum, C. P.: Ketogenic Action of Odd Numbered Carbon Fatty Acids, *J. Biol. Chem.* 136: 503, 1940.
7. Schoenheimer, R.: *The Dynamic State of Body Constituents*, Cambridge, 1942, Harvard University Press.
8. Kass, E. H.: Occurrence of Normal Serum Gamma-Globulin in Human Lymphocytes, *Science* 101: 337, 1945.
9. Janeway, C. A.: Clinical Use of Products of Human Plasma Fractionation: Albumin in Shock and Hypoproteinaemia; Gamma-Globulin in Measles, *J. A. M. A.* 126: 674, 1944.
10. Sachar, L. A., Horvitz, A., and Elman, R.: Studies on Hypoalbuminemia Produced by Protein Deficient Diets; Hypoalbuminemia as Quantitative Measure of Tissue Protein Depletion, *J. Exper. Med.* 75: 453, 1942.

11. Butler, A. M., and Talbot, N. B.: Medical Progress; Parenteral Fluid Therapy; Estimation and Provision of Daily Maintenance Requirements, *New England J. Med.* 231: 585, 621, 1944.
12. Malnutrition During Convalescence; prepared under direction of the Committee on Convalescence and Rehabilitation of the National Research Council, *War Med.* 6: 1, 1944.
13. Brunschwig, A., Clark, D. W., and Corbin, N.: Symposium on Abdominal Surgery; Postoperative Nitrogen Loss and Studies on Parenteral Nitrogen Nutrition by Means of Casein Digest, *Ann. Surg.* 115: 1091, 1942.
14. Metcalf, J., and Stare, F. J.: The Physiologic and Clinical Significance of Plasma Proteins and Protein Metabolites, *New England J. Med.* 236: 26, 1947.
15. Noble, R. P., and Gregersen, M. I.: Blood Volume in Clinical Shock. I. Mixing Time and Disappearance Rate of T-1824 in Normal Subjects and in Patients in Shock; Determination of Plasma Volume in Man from 10-Minute Sample, *J. Clin. Investigation* 25: 158, 1946.
16. Ravdin, I. S., Stengel, A., Jr., and Prushankin, M.: Control of Hypoproteinemia in Surgical Patients, *J. A. M. A.* 114: 107, 1940.
17. Meyer, K. A., and Kozoll, D. D.: Protein Deficiency in Surgical Patients, *Surg., Gynec. & Obst.* 78: 181, 1944.
18. Madden, S. C., and Whipple, G. H.: Plasma Proteins: Their Source, Production, and Utilization, *Physiol. Rev.* 20: 194, 1940.
19. Thompson, W. D., Ravdin, I. S., and Frank, I. L.: Effect of Hypoproteinemia on Wound Disruption, *Arch. Surg.* 36: 500, 1938.
20. Mulholland, J. H., Co Tui, Wright, A. M., Vinci, V., and Shafroff, B.: Protein Metabolism and Bed Sore, *Ann. Surg.* 118: 1015, 1943.
21. Co Tui, Wright, A. M., Mulholland, J. H., Galvin, T., Barcham, I., and Gerst, G. R.: The Hyperalimentation Treatment of Peptic Ulcer With Amino-Acids (Protein Hydrolysate) and Dextri-Maltose, *Gastroenterology* 5: 5, 1945.
22. Cannon, P. R., Wissler, R. W., Woolridge, R. L., and Benditt, E. P.: Relationship of Protein Deficiency to Surgical Infection, *Ann. Surg.* 120: 514, 1944.
23. Brand, E., Kassel, B., and Saidel, L. J.: Chemical, Clinical, and Immunological Studies on the Products of Human Plasma Fractionation. III. Amino-Acid Composition of Plasma Proteins, *J. Clin. Investigation* 23: 437, 1944.
24. Elman, R.: Parenteral Alimentation in Surgery, New York, 1946, Paul B. Hoeber, Inc.
25. Madden, S. C., Bassett, S. H., Remington, J. H., Martin, F. J. C., Woods, R. R., and Shull, F. W.: Amino Acids in Therapy of Disease; Parenteral and Oral Administrations Compared, *Surg., Gynec. & Obst.* 82: 131, 1946.
26. Womack, M., and Rose, W. C.: Evidence for the Existence of an Unidentified Growth Stimulant in Proteins, *J. Biol. Chem.* 162: 735, 1946.

- 27 Woolley, D. W.: Some Correlations of Growth-Promoting Powers of Proteins With Their Strepogenin Content, *J. Biol. Chem.* 162: 383, 1946.
- 28 Sprince, H., and Woolley, D. W.: The Occurrence of the Growth Factor Strepogenin in Purified Proteins, *J. Am. Chem. Soc.* 67: 1734, 1945.
- 29 Varco, R. L.: Preoperative Dietary Management for Surgical Patients, *Surgery* 19: 303, 1946.
- 30 Stare, F. J., and Thorn, G. W.: Protein Nutrition in Problems of Medical Interest, *J. A. M. A.* 127: 1120, 1945.
- 31 Elman, R.: Practical Use of Amino Acids in Protein Nutrition, *J. A. M. A.* 128: 659, 1945.
- 32 Clark, J. H., Nelson, W., Lyons, C., Mayerson, H. S., and DeCamp, P.: Chronic Shock: The Problem of Reduced Blood Volume in the Chronically Ill Patient. In Three Parts, *Ann. Surg.* 125: 618, 1947.

## CHAPTER 4

### SEDATIVE MEDICATION

Even persons who have no difficulty in sleeping under ordinary circumstances may require some type of sedation to induce proper rest while they are in a hospital. Reassurance and a friendly interest by the medical and nursing staffs usually will help to allay mental unrest, but medication should not be withheld if there is the slightest indication for it. The calm and confident patient actually requires less anesthetic during an operation and has a far smoother convalescence than the one who is nervous, worried, and perhaps even convinced of impending death. If sedation alone is required, either triple bromides or sodium bromide will prove satisfactory in doses of 1.0 Gm. (gr. 15) one to three times a day. These drugs help to reduce general nervousness but act only as mild sedatives and are without hypnotic or analgesic effect. The dose is given in two to three ounces of water or milk after meals. Symptoms of bromide intoxication, such as skin rash, nausea, coryza, or mental confusion, may appear in sensitive patients or in those who have previously been taking the drug for long periods of time. Bromides are used only in generally healthy patients and are contraindicated in the presence of tuberculosis or debilitating disease.

A similar sedative effect may be achieved by the use of phenobarbital, 0.03 Gm. (gr.  $\frac{1}{2}$ ), two or three times a day as needed. If it is used frequently over a long period of time, this drug is likely to produce untoward associated symptoms such as mental confusion and lassitude, since it is excreted slowly and tends to accumulate in the body.

Mild sedation alone may not be sufficient to induce sleep in a distressed patient; for this purpose more powerful sedatives or hypnotics must be used.

#### Hypnotic Drugs

Chloral hydrate is an effective hypnotic, time honored and safe. In amounts of 0.5 to 2.0 Gm. (gr.  $7\frac{1}{2}$  to 30) it induces restful sleep somewhat more rapidly than the barbiturates

(fifteen to twenty minutes) but does not maintain it as long (three to four hours). There is usually no headache, drowsiness, or "hangover" the following day. The drug sometimes is irritating to the gastric mucosa and may produce slight nausea, effects which may be diminished by giving it with hot milk. Some patients, particularly children, object to the taste of chloral hydrate. Under these circumstances, it may be given in solution in combination with a flavored vehicle such as syrup of orange or of citric acid to disguise the taste or it may be given as a retention enema in warm milk, starch water, or oil in doses of 0.3 to 2.0 Gm. (gr. 5 to 30), depending on the age of the patient. Disadvantages of chloral hydrate include its irritating effect upon the gastric mucosa and occasional tendency to cause nausea and its mild depressant effect upon respiration. It is rarely toxic in therapeutic doses, although continued use may produce such symptoms as dizziness and headache. Of some importance is the fact that chloral hydrate and alcohol produce toxic symptoms<sup>1</sup> when administered together; chloral hydrate therefore must not be given in association with any compound containing alcohol. Its use also is contraindicated in patients with severe cardiac disease or with disease of the liver, kidneys, or stomach. The conjugation product of chloral hydrate, excreted in the urine, gives a false positive sugar test with Fehling's solution but not with Benedict's solution.

**Paraldehyde**, a polymer of acetaldehyde, is prompt and effective in action and very low in toxicity. Usually given in doses of 3 to 10 c.c. on crushed ice or in syrup of cinnamon orally or in doses of 10 to 30 c.c. well diluted with water or dissolved in olive oil as a retention enema, paraldehyde produces no untoward reactions except, very rarely, mild excitement. This drug is objectionable to the patient because of its characteristic pungent and disagreeable odor. Since the drug is eliminated partially through the lungs, the odor persists in the exhaled air for a relatively long time. In spite of this fault, paraldehyde is a very useful hypnotic.

**Barbiturates.**—The most popular and dependable hypnotics are the drugs of the barbiturate group, of which a fairly large number are available both as U.S.P. and as proprietary preparations. There are differences in physiologic and phar-

macologic effects according to differences in chemical structures, so that choice of a particular barbiturate drug depends upon the effect desired. All barbiturates are potentially habit forming and regular administration over long periods is undesirable.

Members of the longer-acting *barbital* group induce sleep rather slowly, requiring one and one-half to two hours to produce their initial effect, but the sedation is of long duration. Some patients may experience drowsiness and headache during the following day because of incomplete elimination of the drug. *Barbital* is insoluble in water; it is given usually in doses of 0.3 to 0.6 Gm. (gr. 5 to 10), preferably followed by hot milk. The other long-acting member of the *barbital* group in general use, and perhaps the most popular, is *phenobarbital*, which is administered in an average dose of 0.1 Gm (gr.  $1\frac{1}{2}$ ) to induce sleep. If it is used frequently over a long period of time, this drug is likely to produce mental confusion, lassitude, and headache, since it is excreted slowly and tends to accumulate in the body. Many barbiturates may be obtained as the free compound or as the sodium salt; each has its advantages. For example, the sodium salt of *phenobarbital* is water soluble and can be obtained in sterile form in ampules for subcutaneous injection in patients who cannot take it by mouth. The dosage of sodium *phenobarbital* is 0.1 to 0.3 Gm. (gr.  $1\frac{1}{2}$  to 5).

Barbiturates producing effects of intermediate duration, such as the proprietary forms *Amytal*, *Dial*, *Ipral*, *Neonal*, and *Alurate*, are also given in doses of 0.1 to 0.2 Gm. (gr.  $1\frac{1}{2}$  to 3). These drugs act somewhat more quickly than *barbital* and *phenobarbital* and are eliminated more rapidly, so that the effect, while more intense, is of shorter duration.

Short-acting barbiturates produce a hypnotic effect within an hour or less and are eliminated from the body within several hours after absorption. A restful sleep of normal duration, without residual effects the following day, is usually produced. Short-acting barbiturates include *Seconal*, *Nembutal* (pentobarbital), *Amytal Sodium*, *Pernoston*, *Phanodorn*, and other similar N.N.R. compounds. An average dose of 0.1 Gm. (gr.  $1\frac{1}{2}$ ) of any of these drugs is almost always sufficient to produce a sedative effect within an hour; if no effect is noted by that time, the dose may be repeated.

Barbiturates when used together with codeine or aspirin for pain of mild to moderate degree combined with insomnia are more effective than either drug used separately.

As a rule, no toxic effects are produced by any member of the barbiturate group given in therapeutic doses. Longer-acting drugs are eliminated through the kidneys with little or no change and therefore are retained for abnormally long periods if renal damage is present. Barbital and phenobarbital consequently are not the best hypnotics for patients with impaired kidney function. The members of the short-acting group of barbiturates are eliminated following alteration in the liver; they are probably contraindicated in patients with impaired liver function.<sup>2</sup> Drugs of the intermediate-acting group are partly eliminated by the kidneys and partly destroyed in the liver.

For sedation alone, the most commonly used barbiturate is phenobarbital; for induction of restful sleep (hypnosis), members of the intermediate or short-acting groups are probably to be preferred. As simple hypnotics, there is little choice between the various members of each group; any one of a group will serve as well as any other in the same group. If sustained hypnotic effect is desired throughout the night, any member of the longer-acting or intermediate groups will suffice. If the patient's difficulty is only in getting to sleep and not in recurrent wakefulness during the night, one of the short-acting barbiturates is most suitable. A patient may exhibit varying side reactions to one or more barbiturate drugs, such as wakefulness, unpleasant dreams, and mental confusion, particularly if the hypnotic is taken without an analgesic in the presence of pain.

*Overdosage* with barbiturates produces medullary depression, with depression of the respiratory and vasomotor centers and reduction in general body metabolism and in body temperature. The patient is comatose, with slow shallow snoring respirations and a variable degree of cyanosis, the pulse is soft but may show little or no change in rate, the blood pressure and temperature are subnormal, and general muscular relaxation is profound. The pupils are in mild dilatation and slight nystagmus may be present. Treatment of overdosage includes gastric lavage, catheter aspiration of the trachea, administration of analeptic drugs, intravenous injection of dextrose (5 per cent) solution in amounts of 1,000 to 2,000 c.c. for diuresis, and maintenance of

body heat. Oxygen is always of value and in extreme cases can be given by positive pressure with an anesthesia machine. Analeptic drugs generally used include picrotoxin, given intravenously very slowly in doses of 5 to 20 mg., and Metrazol, given intramuscularly or perhaps preferably intravenously in doses of 0.1 to 0.3 Gm. (10 per cent solution). Coramine is especially useful to stimulate respirations depressed by overdosage of morphine; picrotoxin and Metrazol are preferable in treatment of barbiturate poisoning.

### Analgesic Drugs

When insomnia before operation is due partly to pain, some analgesic drug must be used. The analgesic medication may be used alone or, if sedation also is required for sleeplessness, in combination with hypnotic drugs. Aspirin, 0.3 to 0.6 Gm. (gr. 5 to 10), alone or together with the sedative of choice, is effective in relieving mild discomfort causing insomnia. Amidopyrine, in spite of its therapeutic adequacy, is becoming less popular because of its tendency to produce agranulocytosis in susceptible individuals. More severe pain may require more potent analgesics, such as members of the opium group, either alone or in combination with aspirin.

Opium alkaloids and drugs of similar narcotic and analgesic effect are of great value in the alleviation of all degrees of pain, especially sustained pain, but are all subject to the same disadvantage, that habituation or addiction may be produced. In most cases, these drugs produce not only analgesia or relief from pain, but also a hypnotic effect, characterized by a pleasant general relaxation and euphoria that have a strong appeal especially for chronically ill or mentally disturbed patients. There are still no powerful analgesic or narcotic drugs that are free from the danger of habit formation and therefore all drugs of this class should be used only when definitely indicated. No drug can take the place of a narcotic when a patient is having moderate to severe pain, and full therapeutic doses are to be given for relief, but minor degrees of discomfort can be alleviated by simple analgesic medications, and insomnia without pain requires nothing more than a hypnotic drug. In the case of patients who continually complain and exaggerate their dis-



comforts, it is especially important to evaluate the need for narcotics before prescribing them rather than doing so merely to quiet the patient. Sometimes the hypodermic injection of 0.5 c.c. of sterile distilled water or normal salt solution will serve as a placebo, although even this should be used only occasionally, lest the patient develop a dependence on the idea of hypodermic medication. All narcotic drugs are subject to regulation by the United States Government under the Harrison Narcotic Act.

Crude *opium* is the dried resin obtained from the capsule of the poppy, *Papaver somniferum*. Powdered opium, U.S.P., contains 10 per cent opium alkaloids by weight, so that a dose of 0.1 Gm. (gr.  $1\frac{1}{2}$ ) of powdered opium is approximately equivalent to 10 mg. (gr.  $1/6$ ) of morphine. The drug is not ordinarily used in this form except in combination with other drugs (for example, Dover's powder). Tincture of opium (laudanum) is a 10 per cent solution of opium in an alcoholic vehicle, an oral dose of 1.0 c.c. containing 0.1 Gm. of opium or the equivalent of 10 mg. (gr.  $1/6$ ) of morphine. Tincture of opium is one of the older opiates and is no longer widely used. Opium contains at least twenty-five alkaloids, of which the chief narcotics are morphine and codeine.

*Morphine* is the most useful analgesic drug available to the physician. Relief from pain occurs within three to five minutes when the indicated dose of morphine is given slowly intravenously, within twenty to thirty minutes when given subcutaneously, and in not less than an hour when given by mouth. Morphine alkaloid is insoluble in water and morphine therefore is supplied as the sulfate for parenteral use. The dose is from 5 to 16 mg. (gr.  $1/12$  to  $1/4$ ) hypodermically or 5 to 12 mg. (gr.  $1/12$  to  $1/6$ ) intravenously, depending upon the patient's age, weight, and degree of pain. Morphine is not ordinarily used in children except in treatment of extreme pain; if it is used, the dose should not exceed 4 to 10 mg. (gr.  $1/16$  to  $1/6$ ), according to the child's age and weight. Dosage of morphine, as well as of any other drug, may be determined for children by the application of Clark's rule:

$$\text{Dose} = \frac{\text{Weight of child}}{150} \times \text{Adult dose}$$

This formula determines the dose entirely on the basis of weight in pounds, setting the adult weight at a standard of 150 pounds. It is the simplest and probably the most dependable formula available. If the dose is not sufficient, a second supplementary smaller dose may be given after not less than an hour.

The pharmacologic effects of morphine are exerted throughout the body. Pain perception, especially of continuous pain, is interrupted and emotional disturbances are quieted, although cortical functions are otherwise unaffected. As the pain progressively disappears, a state of euphoric drowsiness develops, the patient becomes calm and relaxed, and a refreshing dreamless sleep may supervene.

Other widespread effects on the visceral physiology occur following administration of morphine. Intracranial pressure may be increased. Various medullary centers are affected; the respiratory center is depressed, with consequent decrease in respiratory rate and rise in blood carbon dioxide content, the vomiting center is sometimes stimulated, the temperature regulating mechanism is depressed, and the cough reflex is depressed. The pulse rate may be slightly elevated, although there is little other effect on cardiac action. Motility of the entire gastrointestinal tract is depressed, but tonus of the musculature of the small intestine is increased.

Clinical indications for use of morphine therefore are limited almost entirely to relief of severe pain, although in occasional instances extreme emotional unrest may justify its use. Because it increases tonus of the small intestine, morphine in frequent small doses has been advocated by some writers as an adjunct in the treatment of paralytic ileus. Morphine is less dependable when pain is due to smooth muscle spasm, as in biliary or renal colic, since the drug tends to increase smooth muscle tonus. The depressant effect of morphine on the cough reflex is of great value when the cough is nonproductive or when coughing causes pain, but it is sometimes detrimental in the early postoperative period when accumulating bronchial secretions are likely to contribute to the development of atelectasis.

Contraindications to the use of morphine include (1) the presence of an idiosyncrasy, as in patients who are caused to vomit by the central effects of the drug; (2) the presence of respiratory depression, as in patients with pulmonary or thoracic

injury and reduction of vital capacity or in patients whose respiratory rate is already less than 12 per minute, (3) the presence of actual or imminent increase in intracranial pressure, as in a patient with head injury or intracranial disease, or in a patient being prepared for neurologic surgery; and (4) the presence of undiagnosed acute disease, in which the location and the characteristics of the pain afford diagnostic clues.

Overdosage with morphine is evidenced by stupor, with little reaction to painful stimuli. Respirations are very slow and shallow, pupils are constricted, and the patient may exhibit a grayish cyanosis. Treatment of morphine overdosage is by administration of analeptic drugs, particularly respiratory stimulants such as atropine, 0.4 to 0.6 mg. (gr. 1/150 to 1/100), and Coramine, 3 to 5 c.c. of 25 per cent solution, intramuscularly or intravenously, repeated as often as necessary, and by administration of oxygen. Oxygen can be given by nasal tube; artificial respiration is instituted if necessary and is continued without interruption until the patient's respiratory rate is satisfactory.

*Codeine* (methyl morphine), the least potent of the narcotic drugs, has little or no sedative or hypnotic effect and is most useful in the alleviation of less severe degrees of pain and in the management of painful, protracted, and nonproductive cough. Under these circumstances, and in diabetic patients, it is used as a substitute for morphine. Codeine is usually supplied as the sulfate for oral use. The phosphate is preferred for parenteral administration because of its greater water solubility. Codeine is given for pain in oral doses of 0.016 to 0.06 Gm. (gr.  $\frac{1}{4}$  to 1), preferably with aspirin, and it may be given hypodermically in similar doses. Codeine is about one-sixth as effective as morphine in the relief of pain. For suppression of cough, codeine is effective in doses of 0.008 to 0.03 Gm. (gr. 1/8 to 1/2), either alone or in a cough mixture. Codeine, in doses of 0.004 to 0.03 Gm. (gr. 1/16 to 1/2), according to the patient's age and weight, is effective for relief of pain in children. Infants and children up to 2 years of age respond well to the administration of paregoric (compound tincture of opium) in doses of 2 to 8 c.c. (dr.  $\frac{1}{2}$  to 2).

*Dihydromorphinone hydrochloride*, U. S. P. (Dilaudid, N. N. R.), a synthetic keto derivative of morphine, is as effective as morphine in relief of pain but may also induce habituation and

addiction when used frequently. It is about five to six times more potent than morphine and also is more toxic. Only a small dose of Dilaudid is required for therapeutic effect; it is given hypodermically usually in doses of 2 to 4 mg. (gr. 1/32 to 1/12), equivalent to morphine, 10 to 32 mg. (gr. 1/6 to 1/2).

For continued relief of pain, morphine, Dilaudid, or codeine may be given in effective doses as often as every four hours. Because of the respiratory depression induced by these drugs, further administration is not advisable if the respiratory rate drops below 12 per minute, which is sufficiently below normal to indicate that respiratory depression and some degree of anoxia already are present. The time interval between doses is increased as soon as possible to prevent development of dependence upon the drug.

*Meperidine hydrochloride*, U. S. P. (Demerol, N. N. R.), is a synthetic compound unrelated to morphine but exhibiting to a lesser degree the analgesic properties of morphine as well as the antispasmodic effects of atropine. Its analgesic effects are between those of morphine and of codeine and are of shorter duration.

Various clinical reports<sup>3,4</sup> have indicated that Demerol may be used as an effective substitute for morphine in preoperative sedation or in relief of pain due to any cause, with the advantage that it produces less undesirable side effects than morphine. It does not have the pronounced sedative effect of morphine, however, and has less effect upon apprehension and restlessness. Demerol appears to be of particular value for relief of pain due to spasm or colic, in which morphine is relatively less effective. Dizziness, dryness of the mouth, increased perspiration, nausea and vomiting, and generalized tremors are among the untoward reactions that may be noted and are especially likely to occur in ambulatory patients. Demerol does not produce constipation, has no effect upon the cough reflex, and ordinarily does not produce respiratory depression except in patients with intracranial lesions. Its use in patients with intracranial disease therefore is contraindicated. While Demerol produces nausea and vomiting in some instances, its tendency to do so is less than that of morphine. It may be used therefore as a substitute for morphine when administration of morphine causes vomiting. Disadvantages of Demerol are that some variability

in dosage requirements is noted among different patients, so that rapid and sure relief of pain is not always achieved as promptly as with morphine, in many cases, relatively large doses must be given and repeated at frequent intervals to obtain relief from pain, and in other instances morphine is required in addition for sedative effect in nervous patients. Habituation, although occurring less frequently than with morphine, may follow repeated administration of the drug. Demerol therefore is subject to Federal narcotic regulations.

Doses of 50 to 100 mg. of Demerol, given orally or intramuscularly, are sufficient to relieve moderate degrees of pain, while severe pain may necessitate administration of 150 to 200 mg. of the drug. For relief of continuous or prolonged pain, full doses may be given repeatedly at three- or four-hour intervals. Subcutaneous (hypodermic) administration sometimes causes painful local irritation and is not advised. This drug is likely to cause untoward side reactions when administered intravenously.

*Pantopon*, a purified extract of the opium alkaloids as hydrochloride salts in the natural proportions, offers very little advantage over morphine. Occasionally a patient in whom morphine produces nausea is able to take Pantopon, possibly because of the antispasmodic effect of the contained papaverine. Pantopon contains about 50 per cent morphine and is given hypodermically in a dose of 20 mg. (gr. 1/3).

### Preoperative Sedation

Preanesthetic medication is a preparatory measure of the greatest importance. Administration of sedative drugs before a surgical procedure will quiet an apprehensive and fearful patient, restore calm and increase confidence, and decrease significantly the mortality and morbidity due to the anesthetic. Laboratory experiments have supported clinical impressions in demonstrating that much less ether is needed to induce anesthesia and more than twice as much ether is required to produce respiratory paralysis in animals that have received preanesthetic medication. The conclusion may be drawn that preoperative medication in proper doses will minimize the excitement stage of anesthetic induction, decrease the anesthetic requirement, and reduce the tendency to postoperative pulmonary complications.

An overdose of the sedative, however, may produce a dangerous and prolonged postoperative stupor.

Inhalation anesthetics are particularly likely to produce irritation of the respiratory tract, with consequent excess secretion of mucus and of saliva. Parasympathetic depressant drugs therefore are given preoperatively in conjunction with sedatives, both to decrease the amount of secretion produced in the respiratory tract during anesthesia and to counteract the respiratory depression resulting from sedation.

A wide choice of drugs for preliminary medication is available. Probably the most generally popular is the combined use of a sedative drug given the night before, and possibly repeated the morning of operation, with morphine and atropine or scopolamine hypodermically an hour before induction of anesthesia. The sedative drug is administered at bedtime the night before operation and, if no other preoperative premedication is to be used, again in the morning at least an hour before time of operation. A hypnotic drug with a rapidly developing but briefly sustained action, such as Seconal or Nembutal, is most appropriate. As a rule, a dose of 0.1 Gm. (gr.  $1\frac{1}{2}$ ) of either drug is sufficient for an adult, although twice this amount can be given with safety. Children rarely need the night dose of a preanesthetic hypnotic, but it is advisable to give it an hour before induction of anesthesia, especially local anesthesia. Smaller doses are used for children; a 4-year-old child may be given 16 mg. (gr.  $\frac{1}{4}$ ) of Nembutal or of Seconal orally or twice that amount rectally. The dose is increased by 16 mg. (gr.  $\frac{1}{4}$ ) for each 2 years beyond 4 up to the age of 10 years, at which age the dose is 64 mg. (gr. 1), given either orally or rectally.

The preanesthetic sedative is always given at least an hour before induction of anesthesia, so that the hypnotic effect of the drug is at a maximum when administration of the anesthetic is begun. In this way, sleep merges uninterruptedly into surgical anesthesia with a minimum of disturbance to patient and to anesthetist.

Morphine sulfate and atropine sulfate (or scopolamine) are given hypodermically approximately an hour before induction of anesthesia. These drugs are used either as supplements to, or in place of, the barbiturate given as preoperative sedative. If given alone, morphine and atropine may not sufficiently

decrease the general nervousness of a particularly excitable patient, and under these circumstances a barbiturate also is used. The usual preanesthetic dose for an adult varies according to the preference of different anesthetists. The most generally used combination is morphine 16 mg. (gr.  $\frac{1}{4}$ ) and either scopolamine or atropine 0.4 to 0.6 mg. (gr.  $\frac{1}{150}$  to  $\frac{1}{100}$ ). Others prefer to use morphine in a dose of 10 mg. (gr.  $\frac{1}{6}$ ) combined with scopolamine or atropine, 0.3 to 0.4 mg. (gr.  $\frac{1}{150}$  to  $\frac{1}{200}$ ).

Morphine is especially useful preoperatively in patients who have actual pain as well as apprehension. This drug depresses pain perception, decreases anxiety, and depresses the cough reflex, but it also depresses respiration in both rate and amplitude, decreases the heart rate by its stimulating effect on the vagus center, stimulates the vomiting center, and increases the tonus of smooth muscle in the intestines, vesical sphincter, and biliary tract. While morphine serves well to reduce pain and allay apprehension, its other pharmacologic effects may contraindicate its use at times. Morphine is not entirely safe for use in children, in whom its effects are occasionally irregular and unpredictable. When the patient's vital capacity or respiratory rate is lowered, morphine is not used except in small doses. Morphine is not well tolerated by some patients, causing violent attacks of nausea and vomiting. For this reason, it is not ordinarily used in neurosurgical patients, especially those being prepared for operation, in whom a sudden rise in intracranial pressure might have disastrous effects. Finally, respiratory depression secondary to morphine occasionally may interfere with the anesthetist's evaluation of the patient and may contribute to the development of anoxia during the immediate postanesthetic recovery period. In spite of these disadvantages, morphine is one of the most useful drugs available to the surgeon when used with proper appreciation of all its pharmacologic effects.

Scopolamine and atropine are parasympathetic inhibitors or depressants used chiefly to decrease the amount of salivary and bronchial secretions and to antagonize the respiratory depressant effect of morphine. Both scopolamine and atropine have an antispasmodic effect as well. There is little difference between the two with respect to efficacy as preanesthetic medi-

cation; scopolamine, however, is somewhat more effective than atropine in antagonizing the respiratory depressant effect of morphine, and it also tends to reduce emotional disturbances and often even to induce amnesia. Scopolamine is a cortical depressant, while atropine tends to induce some cortical stimulation. Either drug alone may excite a patient who is having pain and therefore should not be used in such patients unless morphine is given at the same time. Idiosyncrasy to both scopolamine and atropine is not uncommon, the patient sometimes exhibiting excitement of a marked degree. Within these limits, scopolamine and atropine are very useful in preanesthetic medication. It should be noted that scopolamine tends to deteriorate and that a fresh preparation should always be used.

Under certain circumstances morphine may be given intravenously by preference. Occasionally a patient will be brought to the operating room without previous sedation, and morphine will be ordered at that time, or perhaps a small preanesthetic dose of morphine, 8 to 10 mg. (gr.  $1/8$  to  $1/6$ ), may have proved insufficient. In either case, slow intravenous administration of 8 to 10 mg. (gr.  $1/8$  to  $1/6$ ) of morphine sulfate over a period of several minutes will produce a satisfactory response within ten minutes. Administration of additional doses of morphine is dangerous, however, if less than an hour has passed since a dose was given hypodermically. If a second dose is administered before the first dose has been absorbed into the circulation, the cumulative effect on respiration may appear during the course of the operation while the patient is under surgical anesthesia. This effect is particularly dangerous in patients with all degrees of surgical shock.

Preoperative sedation is fully as necessary before operations under local, regional, or spinal anesthesia as it is before operations under inhalation anesthesia. The patient may be even more apprehensive if he knows he is not to be given a general anesthetic, and nervousness and restlessness during the course of the operation will interfere with the conduct of the procedure. Moreover, Tuohy<sup>2</sup> states that the barbiturates tend to balance and prevent any untoward effects of the local anesthetic agents. Preliminary medication also is advantageous before administration of an intravenous anesthetic to reduce excitement and consequently to decrease the anesthetic requirement and improve



the course of anesthesia. Morphine is of less value as preliminary medication for intravenous anesthesia, although atropine, which depresses the vagus and the laryngeal reflexes, should be given in the usual dose. Seconal or Nembutal (0.1 Gm., or gr.  $1\frac{1}{2}$ ) usually will be sufficient for sedation before local, spinal, or intravenous anesthesia.

**Tribromethanol (Avertin).** In certain cases when excitement is great, as in severe hyperthyroidism, or when deep anesthesia is undesirable, as in intracranial operations, a deeper and more prolonged preanesthetic hypnotic effect is desired. Doses of morphine in excess of 16 mg. (gr.  $\frac{1}{4}$ ) or of barbiturates in excess of 0.2 Gm. (gr. 3) are potentially dangerous, so that these drugs alone may not be satisfactory for immediate preanesthetic use. Tribromethanol (Avertin), which is more accurately termed a basal anesthetic agent than a preliminary hypnotic, is of particular value under such circumstances. The drug is supplied as a solution of tribromethanol in amylene hydrate (1.0 Gm. in each 1.0 c.c.) and is administered by rectal instillation. The dose varies from 60 to 100 mg. per kilogram of body weight according to the age, sex, weight, and general health of the patient and according to the type of operative procedure proposed. The usual dose is 60 mg. per kilogram, although in children or in adults with hypermetabolism doses of 80 to 100 mg. are better.

The dose is prepared as a 3 per cent solution in distilled water previously heated to 98° F. and is tested for stability by the addition of a drop or two of Congo red. Decomposition of Avertin releases hydrobromic acid; in concentrations sufficient to depress the pH of the solution below 5, this acid will turn Congo red to purple. Such a reaction indicates that the drug is deteriorating and should not be used. The patient is turned on his side and the solution is administered rectally through a small tube. The liquid is introduced slowly by gravity and care is taken that the entire dose is retained by strapping the buttocks together with a strip of adhesive tape. The catheter is left in place. A responsible attendant must remain with the patient from the time the tribromethanol is given until the anesthetist begins induction of general anesthesia and again after operation until consciousness returns. Effect of Avertin begins within ten minutes and may result in respiratory obstruction if the patient is supine and the tongue drops back into the pharynx. Following

operation, cyanosis may develop and respirations cease unless the pharyngeal airway is kept open by upward traction on the patient's chin.

Avertin is not given to patients with disease of the liver, kidneys, or colon, chronic pulmonary disease, hypertension, hypothyroidism, shock, toxemia, or sepsis or to patients exhibiting cachexia, dehydration, or acidosis, or to patients in the old age group. Within these limits, this drug is a hypnotic agent of very great value. Its use has been advocated in the treatment of tetanus, in which the exhausting spasms may be partially relieved by repeated doses of Avertin.

**Choice of Anesthetic Agent.**—Properly, choice of the anesthetic method to be employed is arranged by consultation between the surgeon and the anesthetist; as a rule, neither should decide without the assent of the other.

Certain physiologic factors influence the use or omission of preanesthetic sedation and the choice of anesthetic agent.

A calm well-sedated patient in a normal physiologic state and not suffering from pain exhibits little excitement during anesthetic induction, and maintenance of surgical anesthesia is smooth, requiring a minimum amount of the anesthetic drug. The presence of certain conditions regularly interfere with proper induction and course of anesthesia. Increased metabolic rate, whether due to hyperthyroidism or to fever (the basal metabolic rate is elevated about 7 per cent for each degree of fever), increases the need for oxygen and consequently increases the percentage of oxygen required in the anesthetic mixture. Emotional unrest, whether due to pain, fear, or hypermetabolism, causes resistance to induction of anesthesia. The resulting excitement increases reflex excitability, raises the oxygen requirement, and also increases the total amount and concentration of anesthetic agent necessary. Children normally have a slightly higher metabolic rate and a very much higher emotional excitability than adults. Obese patients, muscular patients, and patients with short, thick necks are traditionally more difficult to anesthetize because their upper air passages are more easily obstructed. They are therefore more likely to develop subsequent postanesthetic complications. Aged patients, exhibiting generally lowered metabolic rates, are more sensitive to anoxia

and require a high concentration of oxygen during induction and course of anesthesia.

Each anesthetic agent has certain fairly definite indications and contraindications.

*Nitrous oxide* is an anesthetic gas which produces almost no direct toxic effects. However, unless the patient is well sedated, nitrous oxide must be given with such low concentrations of oxygen that it becomes unsafe. Its chief use is in production of unconsciousness rapidly and not unpleasantly, after which other anesthetic agents, particularly ether, are substituted.

*Ethylene*, also a relatively nontoxic anesthetic gas, provides somewhat deeper anesthesia than does nitrous oxide. Induction is rapid and not unpleasant, and the drug produces little or no reaction during the recovery period. Preoperative sedation is of particular value because of its effect in lowering the patient's oxygen requirement. As a rule, percentages of ethylene averaging close to 80 are required to induce surgical anesthesia. For this reason and also because muscular relaxation is incomplete during ethylene anesthesia, ether vapor usually is added as a supplement. For short operations in which complete relaxation is not necessary, ethylene is an excellent anesthetic. Its chief disadvantage is the possibility of production of anoxia; an added disadvantage is the fact that it is highly explosive.

*Cyclopropane* is a powerful anesthetic gas, affording pleasant rapid induction and smooth maintenance of deep surgical anesthesia. A high concentration of oxygen may be given in conjunction, so that anoxia is never a problem. Toxicity of cyclopropane is low, although there is considerable evidence that cardiac irregularities may be produced. Vasoconstrictor drugs such as epinephrine (Adrenalin) or Neosynephrine increase the frequency of occurrence of cardiac irregularities during cyclopropane anesthesia<sup>1</sup> and therefore are never used in conjunction with it. Cyclopropane is of the greatest value when a high percentage of oxygen is necessary during anesthesia. It is a very suitable anesthetic for thoracic surgery and for surgery in patients with pulmonary disease, anemia, anoxia, or pregnancy, in all of whom the oxygen requirement is higher than usual. It is probably better avoided in patients with cardiac disease, particularly with disorders of rhythm, or with disturbances of the blood pressure.

since a rise in blood pressure may occur during administration of cyclopropane as well as a fall in pressure during recovery. Its only other dangerous attribute is its explosive nature, so that cyclopropane usually is not given during an operation in which the use of a cautery or an electrosurgical unit is contemplated.

*Ether* (diethyl oxide) is the safest general anesthetic available, particularly if the anesthetist has had a minimum of training. Because induction of anesthesia with ether is slow and unpleasant and because ether vapor is irritating to the respiratory tract, induction usually is accomplished with a rapidly acting, non-irritating anesthetic such as ethylene, cyclopropane, or even intravenous sodium pentothal. Preanesthetic sedatives and parasympathetic depressant drugs (atropine, scopolamine) are of the greatest value in preparation of the patient for ether anesthesia. Toxicity of ether is low in anesthetic doses and it is a safe drug for the average patient as well as for patients with cardiac disease and for infants and young children. Ether tends to cause acidosis, vomiting, pulmonary irritation, and occasionally a reduction in liver function. It is not used if acidosis or a tendency to acidosis is present, as in diabetes, or if disease of the respiratory tract, such as chronic bronchitis, bronchiectasis, or pulmonary tuberculosis, is present.

*Chloroform*, which provides a rapid and easy induction of general anesthesia, is no longer widely used in the United States for this purpose because of its dangerous tendency to cause severe cardiovascular depression, ventricular fibrillation, progressive central necrosis in the liver, and fatty degeneration in the kidneys. Chloroform sometimes is used to provide rapid induction for subsequent ether anesthesia. It is also used occasionally in small quantities as an adjuvant to nitrous oxide or to produce light narcosis.

*Spinal anesthesia* is of most advantage in healthy young or middle-aged patients who are not apprehensive, or in older patients in whom the use of general anesthetics may be dangerous (diabetic gangrene, etc.). Use of spinal anesthesia is contraindicated in apprehensive or excitable patients and in patients with disease of the cardiovascular or central nervous system or with abnormally high or low blood pressure. The chief advantages of spinal anesthesia<sup>6</sup> include the high degree of muscular

relaxation produced, the ease of administration, the smooth course and recovery period, and the lack of effect upon the body metabolism.

The chief disadvantages include its tendency to depress respiration and blood pressure, its tendency to produce nausea and vomiting during anesthesia, and its tendency to increase the patient's susceptibility to operative shock. Progress of the anesthetic agent up the spinal canal produces a varying degree of paralysis of the thoracic motor nerves, with consequent diminution of thoracic respiratory excursions. By its effect on the anterior nerve roots within the spinal canal, a spinal anesthetic drug produces a constant but variable degree of paralysis of the vasoconstrictor nerve fibers, with a consequent fall in blood pressure. An additional causative factor in the blood pressure drop may be the relaxation of the skeletal muscles induced by the anesthesia, with local pooling of fairly large quantities of blood. Because the compensatory reflexes cannot operate properly in a patient under spinal anesthesia, sudden or protracted hemorrhage or trauma may initiate shock earlier than would be expected in the case of general anesthesia. However, hypotension resulting from spinal anesthesia responds readily to sympathetic stimulant drugs. The patient's blood pressure is read and recorded at intervals of five minutes during the operation and a dose of a stimulant drug is given intravenously if a fall in blood pressure develops. Ephedrine, 45 mg. (gr.  $\frac{3}{4}$ ) or Neosynephrine hydrochloride, 3 to 6 mg. (0.3 to 0.6 c.c. of 1.0 per cent solution), or Methedrine hydrochloride<sup>7</sup> (d-desoxyephedrine), 20 mg., may be used. Oenethyl (2-methylaminoheptane), one of the newly introduced aliphatic amines, has been investigated by Roman-Vega and Adriani<sup>8</sup> with respect to use as a vasopressor substance for spinal anesthesia. The writers find this drug to be safe and effective both prophylactically and therapeutically. The average dose suggested for intramuscular use is 75 to 100 mg., and for intravenous use, 25 to 50 mg.; given in divided fractions of 5 to 10 mg., allowing a lapse of 15 to 30 seconds between each fraction.

**INTRAVENOUS ANESTHETICS.**—Two members of the ultra short acting group of barbiturates (sodium pentothal and sodium evipal) are not commonly used as simple hypnotics but are employed as general anesthetics, administered intravenously.

*Sodium pentothal* is the intravenous anesthetic agent that has found widest use; thousands of operations were performed under sodium pentothal anesthesia during World War II. The drug is given as a 2.5 per cent solution in distilled water, from 0.5 to 1.5 Gm. being used according to the length of the operation and the depth of anesthesia desired. Induction usually requires from one to three minutes. Use of intravenous anesthetic agents is commonly restricted to operations not requiring complete relaxation and not lasting more than thirty minutes. Pentothal does not have a high margin of safety; the anesthetic dose is approximately one-half of the toxic or lethal dose. Intravenous anesthetics are not used in the presence of liver or kidney disease, obstruction or disease of the respiratory tract, anemia, or metabolic disturbance, and they are generally avoided in aged patients. Operations about the head, face, and larynx also are contraindications to the use of intravenous anesthetics, as well as operations during which the patient must lie in the prone position.

### References

1. Goodman, L., and Gilman, A.: *The Pharmacological Basis of Therapeutics; a Textbook of Pharmacology, Toxicology, and Therapeutics for Physicians and Medical Students*, New York, 1941, The Macmillan Co.
2. Adriani, J.: *The Pharmacology of Anesthetic Drugs: A Syllabus for Students and Clinicians*, ed 2, Springfield, Ill., 1946, Charles C Thomas.
3. Hori, C. G., and Gold, S.: Demerol in Surgery and Obstetrics, *Canad. M. A. J.* 51: 509, 1944.
4. Batterman, R. C., and Mulholland, F. H.: Demerol. A Substitute for Morphine in the Treatment of Postoperative Pain, *Arch. Surg.* 46: 404, 1943.
5. Tuohy, E. B.: Anesthetic Procedures Used at the Mayo Clinic. I. General Considerations of Local, Inhalation, and Intravenous Anesthetic Agents and Methods and Premedication, *Proc. Staff Meet., Mayo Clin.* 13: 284, 1938.
6. Eversole, U. H.: Why Use Spinal Anesthesia? *J. A. M. A.* 128: 256, 1945.
7. Dripps, R. D., and Deming, M. Van N.: An Evaluation of Certain Drugs Used to Maintain Blood Pressure During Spinal Anesthesia. Comparison of Ephedrine, Paredrine, Pitressin-Ephedrine and Methedrine in 2,500 Cases, *Surg., Gynec. & Obst.* 83: 312, 1946.
8. Roman-Vega, D. A., and Adriani, J.: The Efficiency of Oenethyl (2, methyl amino heptane) as a Vasopressor Substance for Spinal Anesthesia, *Anesthesiology* 7: 62, 1946.

## CHAPTER 5

### GENERAL PREOPERATIVE MEASURES

The steady reduction of surgical mortality in recent years has been accomplished not only by improvement in technique and in operative procedures, but also by the careful clinical application of well established physiologic principles and by the adoption and utilization of the newer findings in the fields of physiology, biochemistry, and nutrition. It is no longer sufficient for the surgeon to know that his patient has a defect or a pathologic condition that can be removed or corrected by operation; he must also be aware of the changes in function that may be responsible for or that may arise from such a lesion. The associated physiologic disturbances, local and systemic, must be noted and corrected as far as possible before operation is undertaken. Failure to look beyond the lesion itself is often responsible for unnecessary fatalities.

After the nature and extent of the disease requiring surgical intervention have been determined, the general condition of the patient should be estimated. As a rule, those who come to the hospital for an elective operation show little evidence of disturbed physiology unless some unrelated disease is present and has produced systemic changes. On the other hand, patients who are admitted for emergency operations and are suffering from acute infectious, traumatic, or obstructive processes are much more likely to show associated derangements of water and electrolyte balance and a decreased resistance to operative trauma. Patients of this type may exhibit also a tendency to develop postoperative shock and other complications. The same effects may be produced by long-standing visceral disease, chronic anemia, and malignant tumors. In all cases of these types the final outcome depends largely upon the degree to which the associated disturbances are corrected before operation is undertaken and also upon the prevention of postoperative complications.

Certain procedures must be followed in preparing any patient for operation, however minor it may be. Some individuals require much expert and painstaking preparation, while the average

good-risk patient entering for an elective operation usually needs only minimal essential preparatory measures.

**Permission.**—Consent, either verbal or written, is requisite before a surgical operation may be performed upon anyone for any purpose. Forms, such as those advocated<sup>1</sup> by the American Medical Association, may be secured or drawn up by those who prefer the additional legal security of a signed permission slip, although physicians, as a rule, seem reluctant to ask for written authorization.

In the case of children, the permission of the legal guardian is always necessary. In all emergency cases requiring immediate attention, such as acute visceral disease or traffic accidents, first-aid measures may be instituted, but anything beyond simple treatment requires the consent of the patient or, if he is too ill to give it, of his nearest relative. This is especially true of children. Every effort must be made to locate a legally responsible relative, but if, after all attempts fail, the condition still demands immediate care, the surgeon should call in consultation at least one other registered physician to attest later, if necessary, to the lifesaving nature of the procedure. Sometimes, in case of emergency, the hospital superintendent may share the responsibility.

Finally, permission should be obtained before induction of anesthesia to correct any additional pathologic condition that may be discovered during operation. If not, it may become necessary to interrupt the operation while the nearest relative is consulted.

When the patient has been referred by another physician, it is customary to notify the referring doctor, on the day preceding, of the time of operation, so that he may attend the operation and speak to the patient beforehand if he desires. Occasionally, the surgeon may prefer not to inform the patient of the time and date of operation in order to insure sound sleep the night preceding. This is a matter of individual decision in which the personality and general condition of the patient must be taken into consideration. Some responsible member of the family must be notified of the hour of operation under these circumstances.

**Reassurance.**—A stay in the hospital is a new and often terrifying experience for the average person. Recognition of



this state of mind is the surgeon's duty, and a short, reassuring conversation may be of great help. Here, too, a cheerful demeanor and friendly attitude on the part of the nurses and house doctors may mean much to a nervous patient.

Bedside discussions of pathology, procedure, and prognosis among doctors are eagerly followed by the interested patient, who understands a little and misinterprets a great deal. While it is necessary to explain the general principle of a proposed operation to a patient, especially an intelligent one, it is decidedly unwise to go too minutely into the details of the procedures and physiology involved. For example, after about a week of exemplary convalescence following a simple gastroenterostomy, a patient, for no apparent reason, suddenly began to vomit everything taken by mouth. Clinical investigation revealed no cause for the disturbance until the patient, after much persuasion, finally produced a sheet of paper upon which a too obliging house doctor had diagrammed various stomach operations and described how they worked. As a rule, information concerning a patient's state of health and the details of treatment are given only by the physician directly in charge, upon whom the responsibility rests.

**Examination.**—The history and physical examination must be thorough and should be performed and recorded immediately on the day of the patient's arrival. Unnecessary procedures are to be avoided, but any indication of a possible complicating pathologic state should be minutely investigated. Often a serious concurrent disease may be discovered through some apparently minor point in the routine history or physical examination. A history of occasional night sweats may point to undulant fever or to a latent tuberculosis, or slight inequality of the pupils may be the only obvious indication of an early neurosyphilis. Such evidences of associated disease are found only by the careful recording of a full past history and the conscientious performance of a complete physical examination.

The patient's preoperative examination always includes a blood pressure reading, a hemoglobin determination by a reliable method, a white blood cell count, a differential smear, and a careful urinalysis. No anesthetic ever should be administered until a thorough examination of the heart and lungs has been performed and a urinalysis and blood pressure determination re-

corded. It is of the utmost importance that every patient be given this minimal examination before he is subjected either to general or to spinal anesthesia. Discovery of any variation from the normal indicates the necessity for an investigation of the organ or function involved (Chapters 9 and 10).

In special cases certain supplementary tests are mandatory. Diseases accompanied by anemia or by variations in the coagulability of the blood require bleeding and clotting time determinations and sometimes more specialized tests, such as hematocrit readings, blood platelet counts, sedimentation time determination, and prothrombin time estimation (Chapter 9).

The blood Wassermann reaction is to be determined in every case without exception unless such a test has been done elsewhere recently. The widespread distribution of syphilis in all levels of population, its long latent period, and the protean nature of its manifestations all make it impossible to ignore and equally impossible to diagnose without a specific test. In some localities a stool specimen should be routinely examined for parasites; often a puzzling anemia or an obscure abdominal complaint may be explained by the presence of intestinal parasites.

Roentgenologic examinations<sup>1</sup> are made when indicated. Some clinics make a practice of securing a roentgenogram of the chest in every patient who is to receive a general anesthetic. This is especially applicable to children. Other hospitals reserve this precautionary measure for those who show evidence of pulmonary or cardiac disease, either in the past history or in the physical findings. Photographs of a lesion or of a specimen always convey more information than many pages of written description and have long been used as records in plastic work. They are surprisingly simple to secure and may be taken satisfactorily with any folding or miniature type of camera and two adjustable lamps.

Patients occasionally may enter the hospital having already been subjected to certain laboratory or clinical tests. Such examinations need not be repeated if they were done by a reliable laboratory unless sufficient time has elapsed for a significant alteration to have taken place. While unnecessary procedures are annoying to the patient and expensive to perform, no examination that might yield useful information should be overlooked.

Every patient who is about to undergo a serious operation or who is in a generally weakened state from pre-existing disease should be grouped for possible transfusion and cross-matched with suitable donors or blood bank specimens.

**Metabolic Disorders.**—Nutritional deficiencies and moderate dehydration are frequently found; these conditions, if present, must be noted and corrected before operation, as described elsewhere. Replacement of the lacking elements, whether body fluids, electrolytes, blood constituents, or vitamins, will occupy several days and should not be attempted in too hurried a fashion. It is never possible to repair within a span of a few hours the damage produced by an illness of long duration.

Particular attention must be paid to the establishment of a proper fluid and electrolyte balance in the body and to the replenishment of depleted tissue protein and liver glycogen. Body water and salt deficiency states may be recognized and evaluated by examination of the blood and urine. The degree of fluid deficiency can be ascertained without difficulty by charting the daily fluid intake and measuring the urinary output. The total daily urine quantity is probably the most important single check on the adequacy of fluid intake, the optimum output in the absence of cardiorenal disease being approximately 1,500 cubic centimeters. In the average patient fluid replacement may be accomplished by administering from 2,500 to 3,500 c.c. of fluid daily by mouth if possible; otherwise by clysis.

Administration of carbohydrate is of especial importance in individuals exhibiting metabolic diseases or chronic malnutrition. When the glycogen stores of the liver are depleted, the patient is no longer a safe operative risk. Carbohydrates given by mouth are effective in restoring the liver glycogen as well as dextrose given by infusion; consequently, a diet high in carbohydrate and in protein is given for at least several days before operation. When the preoperative period is necessarily short, as in emergency cases, or when oral administration is impossible, dextrose is given by vein as a 5 or 10 per cent solution.

Chronic malnutrition due to starvation also produces some degree of hypoproteinemia and breakdown of body protein. Decrease in plasma proteins is accompanied by a proportionate loss of plasma water to maintain the protein concentration and osmotic tension at a normal level. The total blood volume is

therefore diminished, the relative hemoconcentration serving to disguise the reduction in plasma protein values as well as the usually associated anemia. Administration of carbohydrate or salt solutions is not sufficient to meet the physiologic requirements of these chronically malnourished patients; dilution of the plasma will result, with prompt transudation of water and salt into the tissues. Therapeutic use of crystalloid solutions in a hypoproteinemic patient therefore may result in latent or even clinical edema; proteins also must be supplied. Transfusions of whole blood or plasma are of much value in temporary emergency improvement of body protein deficiency but are insufficient in themselves for restorative therapy. Oral feeding of high protein diets, tube feeding of high protein mixtures, and oral or intravenous administration of protein hydrolysates and amino acid mixtures can accomplish an almost incredible improvement in a debilitated patient's condition within a relatively short time, especially when used in combination with blood transfusions.

The avitaminoses are no longer vague and indefinite syndromes. The effects produced by insufficient intake of each vitamin are now fairly well established, as well as the striking therapeutic results that may be expected through the use of the highly purified or synthetic preparations of the vitamins, when deficiency exists.

**Intercurrent Infections.**—Search should be made for foci of infection, particularly in the respiratory tract, and appropriate treatment instituted for any lesions that may be present. Oral sepsis of marked degree, with purulent infection of teeth and gums, sometimes may be responsible for severe postoperative pulmonary complications. Treatment of the infected mouth should be thorough; the potential gravity of the condition must not be ignored. Acute or subsiding coryza, pharyngitis, or tonsillitis must be looked for in each patient, both by questioning the individual and by physical examination. Operation, as a rule, is postponed for at least one to two weeks following complete disappearance of all evidence of such infections.

Tracheitis or bronchitis is more serious and may require delay of elective operations for even longer periods. Early operation is contraindicated in patients with acute respiratory tract infections, even with the use of spinal or local anesthesia, since these types of

anesthetics are followed by pulmonary complications almost as often as are the inhalation types. The necessity for a thorough examination, especially of the chest, before any anesthetic is administered cannot be emphasized too strongly.

**Specific Measures.**—After the patient has been admitted and the history and physical examination have been recorded, necessary orders are written on the chart. Any restrictions concerning the patient's freedom to be out of bed or to walk about, as well as any isolation measures that may be necessary, as in the case of transmissible infection, should be noted on the order sheet. A suitable diet is prescribed. In general, a full diet may be given until the night before operation, special conditions excepted. After midnight preceding operation the patient receives nothing by mouth except water.

Frequently, patients may lose 1 to 3 liters of fluid by evaporation during prolonged surgical procedures; losses so large are not well tolerated if there is any fluid deficiency. Before serious operations, especially those which are likely to be followed by a period of starvation or vomiting, the patient should be given at least 500 c.c. of normal salt solution and 500 c.c. of 10 per cent dextrose by infusion.

**Preoperative Medication.**—Sedatives may or may not be necessary during the preoperative period, according to the individual patient concerned. It is worth while for the physician to pay attention to this phase of his patient's welfare, however, for all surgical patients are frightened at the prospect of undergoing anesthesia and surgery, no matter how calm and placid they may appear. Inquiries as to how the patient slept the preceding night should be made seriously for informational rather than conversational purposes, and if the patient has not slept well, the proper sedative or hypnotic should be prescribed for the next night. In every case, a hypnotic should be ordered for the night immediately preceding operation and should be given. A tired and anxious patient who has spent a sleepless night does not take anesthesia as well as the patient who has had satisfactory rest, nor does he recover as quickly following operation. Choice of drugs and methods of administration are discussed in Chapter 4.

**Elimination.**—Before the patient is taken to the operating room, the urinary bladder is emptied, especially if an

abdominal operation is planned. Catheterization can usually be avoided but occasionally may be necessary. This routine procedure should never be overlooked, because some operations, especially those upon the structures below the pelvic brim, cannot be performed unless the urinary bladder is empty. If an extra-abdominal operation is contemplated, this consideration is of less importance.

Proper preparation of the bowel requires the administration of a soapsuds enema the night before and again three hours preceding operation. This procedure is necessary before rectal or pelvic operations; one enema is usually sufficient before operations of other types. Cathartics are no longer used for preoperative purgation; they cause an undesirable loss of fluid and tend to weaken the patient. The details of preoperative preparation, as well as the dose and time of administration of preoperative sedatives, are noted on the chart, which should accompany the patient to the operating room.

**Local Measures.**—Any lesions near the field of the proposed operation must be noted on admission and treated appropriately. A furuncle or an infected hair follicle may offer sufficient reason to postpone an elective operation; if local infection is ignored, a wound abscess may develop after operation. A layer of collodion over the lesion, or a tiny patch of sterile gauze covered with collodion, will help to prevent accidental contamination of the operative wound.

The operative field is shaved the night before operation and gross dirt removed from the skin with soap and water and ether. If necessary, this procedure can be postponed until the patient arrives in the operating room and anesthesia is begun. Shaving should be done carefully, without nicking the skin, and the umbilicus, as well as any creases that may be present in the skin, must be cleansed thoroughly. Further preparation and sterilization are done on the wards in special cases and in the operating room, according to the personal preferences of the surgeon.

More complicated procedures for preparing the operative field are sometimes followed. For example, a wide area of skin may be shaved the night before operation and the full routine antiseptic sterilization then performed. The entire region is covered with a sterile towel, which is taped securely to the skin at

the sides. In addition, the usual antiseptic preparation is carried out just before operation. Although methods of this type were widely popular in the past, they are now rarely used. Sterilization of the skin the night before operation is useless because the sterility is not maintained, and close application of a heavy dressing to the skin for twelve to eighteen hours prevents evaporation and encourages maceration.

**Emergency Operations.**—In case of emergency the chief requisite is the saving of a life and the patient may not always be a good risk.

No matter how grave the condition appears, there are really only two conditions which require instant intervention: asphyxiation and hemorrhage. In practically every other emergency the heart and lungs must be examined thoroughly after the probable diagnosis is made and a urinalysis must be performed. With this information, together with a blood pressure reading and a white blood cell count and hemoglobin determination, a satisfactory evaluation of the patient's status can be made and an appropriate plan of procedure outlined. Frequently, plain x-ray films of the chest and of the abdomen may furnish valuable information. If some such plan is followed, medical and urologic conditions which simulate acute surgical diseases of the abdomen may be discovered before a too hasty operation is undertaken. Postoperative pulmonary complications may be foreseen and perhaps prevented if the lungs are examined properly before operation.

If the patient is in or approaching shock, blood transfusions and other restorative measures are prepared and administered while the operating room is being made ready. If there has been any vomiting or if ketones are found in the urine, an infusion of dextrose and normal salt solution is begun. Operation cannot be performed until the tendency to shock is under control. It is never safe to operate upon a patient who exhibits a dangerously low blood pressure and a rapid running pulse; shock is much easier to prevent than to treat.

### References

1. Woodward, W. C.: *Authorization of Physical Examinations, Treatment, Operations and Autopsies*, J. A. M. A., 106: 33, 1936.

## CHAPTER 6

### GENERAL POSTOPERATIVE MEASURES

Postoperative care begins in the operating room, where precautions should be taken by the surgeon to forestall the development of complications. Avoidance of rough and unnecessary manipulation of the intestine will minimize subsequent distention; gentle use of abdominal retractors will reduce trauma to the wound and permit better wound healing; economy of time in operating will decrease postoperative shock; and a minimum of devitalized tissue will lower the incidence of postoperative infection. A small pillow or folded sheet placed under the lumbar curve of the back during operation may prevent subsequent backache, which often results from muscular relaxation and strain while the patient is anesthetized.

**In The Operating Room.**—If the operation is to be a serious one or if the patient is not in good condition, an infusion is begun after anesthesia has been induced and before the patient has been draped for operation. The needle should be large enough (17 to 19 gauge) to permit administration of blood if necessary and is inserted into a superficial vein either by venipuncture or by cannulation. Fixation of a cannula or needle in a vein is preferable if the patient is a poor operative risk and a prolonged operation is likely. If an infusion is not begun before the necessity for it arises, a sudden drop in the patient's blood pressure may cause such a decrease in venous filling that exposure of a vein even through a small incision may be difficult. The best fluid for general use is 5 per cent dextrose in distilled water, administered at a rate of 50 to 75 drops (3 to 5 c.c.) per minute. The routine use of normal salt solution for infusion during operation is not recommended because of the possibility of salt retention and latent edema following operation.

Any fluid or medication given in the operating room must be noted on the patient's chart at the time of administration. This is usually the responsibility of the anesthetist, who also records readings of the patient's blood pressure, pulse rate, and respiratory rate at frequent intervals.



The orders for the patient's care during the first twenty-four hours following operation are written and signed in the operating room and are returned to the patient's room with him. These orders should specify the proper position of the patient, the diet or fluids that can be taken by mouth, the amount, type, and method of administration of fluids by other routes, the dose of analgesic medication, and, if necessary, a repeat order for the medication. Special orders for special patients, such as those with operations on the gastrointestinal tract, must be explicit and full. Other pertinent information noted at this time includes the operation performed, the anesthetic used, and the number and character of the drains. If notation of these orders and data is postponed until the patient reaches his room, some detail may be forgotten.

Wet clothing is changed before the patient is removed from the table. When the patient is transferred to the stretcher, his head must be supported in order to keep it from snapping back and causing a painful cervical sprain. The patient's entire body is carefully covered with a blanket to conserve heat. The heat-regulating mechanism is disturbed by anesthesia and every effort must be made to prevent variations in body temperature, particularly temperature falls to subnormal levels. The face is cleaned and a towel is wrapped around the head. The unconscious patient should be accompanied to his bed by the anesthetist and then must be constantly attended, until consciousness returns, by a nurse familiar with the symptoms and treatment of post-operative obstruction in the air passages.

Preparation of the bed to receive an unconscious patient is a standard routine in most hospitals. If hot-water bags are used to warm the bed, they are all removed before the patient is transferred. When the patient is lifted from the stretcher to the bed, care must again be exerted to prevent injury to the neck or to an arm.

**Recovery From Anesthesia.**—The anesthetized patient is usually placed in the dorsal recumbent position until consciousness returns, but in actual or threatened shock the foot of the bed is elevated from twelve to eighteen inches. No pillow is used until the patient has recovered from the anesthetic. The room should be well lighted, so that the attending nurse can

observe any color changes that develop; the room may be darkened as soon as the patient regains consciousness.

The head should be slightly lowered and turned to one side to prevent obstruction of the airway by the relaxed tongue. If pharyngeal obstruction occurs and respiration becomes difficult, cyanosis may develop rapidly, appearing earliest in the lips and ear lobes. Extension of the patient's neck by elevation of the chin is usually sufficient to restore proper breathing space. Slight hyperextension of the neck should be maintained as long as necessary in those individuals who tend to develop this type of pharyngeal occlusion. When change of position is not immediately effective, the patient's mouth must be opened and the tongue grasped with forceps or with a sponge and pulled forward strongly. Elevation of the chin at the same time will secure maximum opening of the airway. These procedures are more successful than attempts to introduce a metal airway if pharyngeal sensation is returning, since the reflex coughing induced by efforts to pass the airway not only prevents its insertion, but also increases the respiratory distress of the patient.

Aspiration of vomited material and mucoid secretions into the lungs may cause a severe postoperative pneumonia. This accident can be avoided simply by keeping the patient's head flat on the bed and turned to one side for proper drainage.

The semiconscious patient, as a rule, experiences no difficulty in ejecting the stomach contents, but if the pharynx and trachea become clogged with mucus or vomitus, immediate removal of the secretion is necessary. The patient is brought to the side of the bed and the head held downward at a slightly lower level than the body, while the tongue is grasped firmly and drawn forward. In such a position of dependent drainage the patient's pharynx usually will be cleared by the next expiratory effort. If the tongue cannot be seized, the attendant may insert a soft mouth gag to keep the jaws apart. A serviceable instrument of this type may be made by wrapping several wooden tongue depressors together with four or five layers of adhesive tape, to prevent the wood from splintering. Metal mouth gags are not advised since they may break the teeth. A small portable suction apparatus run by an electric motor is most useful in such cases for emptying the pharynx rapidly and efficiently by means of a catheter passed through the mouth or nose. Attempts at sucking out secretions

through a catheter with a syringe attached are not successful as a rule, but this may be attempted when simple postural drainage is not immediately effective and suction equipment is not available.

**Position.**—After the patient has regained consciousness and is no longer in danger of developing shock or of aspirating vomitus, he may be given a pillow and his position changed.

As a rule, the patient is most comfortable in the horizontal position. Prolonged recumbency is likely to be tiring, and occasional changes to *Fowler's position* are restful. Some surgeons prefer to have their patients kept in some variation of Fowler's position more or less constantly, especially following abdominal operations. This position is usually described in three degrees of elevation; in low Fowler's position the distance between the sta-

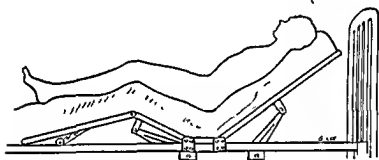


Fig 8—Fowler position. The patient should not be allowed to slump downward, a support beneath the knees is necessary.

tionary horizontal frame of the bed and the movable frame at the head is an arbitrary ten inches of elevation; in mid-Fowler's position the distance is fifteen inches; and in high Fowler's position the elevation is twenty inches. In each case the knees must be elevated either by adjusting the lower half of the bed or by placing a pillow beneath the knees, or the patient will simply slide downward.

Certain advantages have been claimed for the use of Fowler's position. Deeper respirations are encouraged, especially in the presence of abdominal distention. A patient suffering from respiratory embarrassment for any reason is more likely to be comfortable in the sitting position, in which the abdominal contents

tend to gravitate away from the undersurface of the diaphragm. More room is consequently allowed for respiratory excursions. Although the point is open to question, it is widely maintained that Fowler's position is useful in the management of spreading peritonitis when a large amount of exudate is present, both by favoring localization of collections of pus at dependent sites and by minimizing the formation of encapsulated pockets in the upper abdomen, where their presence is most dangerous. Absorption of toxic material from the peritoneal cavity is said to be somewhat decreased in the semisitting position, probably by downward movement of the exudate away from the diaphragmatic region where respiratory movements tend to increase the rate of absorption.

This position somewhat encourages relaxation of the abdominal muscles by relieving tension on the incision and decreasing postoperative pain. For these reasons, it is often favored following abdominal or inguinal hernia operations to reduce tension on the area of repair.

Disadvantages of Fowler's position arise chiefly from the discomforts induced by a prolonged stay in this position. It is best used only as a change from the horizontal position, and its supposed advantages are being accorded much less importance than in former years. Lumbosacral backache may appear in patients kept in Fowler's position too long; proper rest and sound sleeping are difficult in this attitude. Continued pressure on the skin over the sacral region may result in the development of decubitus ulcers in infirm patients; frequent alterations of position, use of a rubber ring, and application of 50 per cent alcohol several times a day may help to prevent pressure sores. It has been suggested that the propped-up position, by creating a puddlelike area of stasis in the pelvic veins and pressure on the popliteal spaces, tends to increase the frequency of occurrence of postoperative venous thrombosis.

It has been suggested,<sup>1</sup> however, that the early use of Fowler's position actually may increase incidence of suprahepatic (subphrenic) space infections in patients in whom infected material is present in the free peritoneal cavity, because the pneumoperitoneum present following laparotomy produces an air bubble which tends to rise above the liver in the propped-up patient. Fluctuations in the air bubble during respiration may

serve to aspirate free fluid from the abdomen up into the subphrenic spaces, with increased danger of local infection. The postoperative pneumoperitoneum disappears after a day or two, and the patient then can assume the position he finds most comfortable. Most surgeons have discontinued routine use of Fowler's position, preferring the horizontal position, at least for the immediate postoperative period. When the patient's condition has shown definite and satisfactory improvement, it is safe to permit any position desired, preferably with frequent changes.

Frequent changes in position improve the circulation generally, encourage deeper respirations, reduce the development of abdominal distention and constipation, and decrease the incidence of postoperative venous thrombosis and pressure sores. For the first day or two after operation, the patient's position should be changed every one or two hours as a routine measure, unless some contraindication is present or unless the patient is asleep. Exercises in bed are of the greatest value in encouraging rapid return of strength, proper ventilation of the lungs, and increased circulatory efficiency. The patient is required to exercise each arm and each leg, both separately and together for stated periods and at frequent intervals during the day, under supervision of a nurse if possible.

Maintenance of an unchanged position for long periods of time occasionally results in temporary disturbances of joints. The nurse must be sure that bedclothes are not pulled down too tightly over the patient's feet; convalescence from a prolonged illness may be followed by foot drop of one or both extremities unless some support such as a pillow under the bed covering is supplied to keep the feet at right angles to the legs. In debilitated patients, foot drop is occasionally seen also following constant pressure on the external peroneal nerve near the head of the fibula.

When there is a large amount of drainage from a wound such as a large abscess or carbuncle, the outflow of exudate may be facilitated by keeping the affected area in a dependent position. In other cases, for example, following a brain operation in which a bone flap has been removed, pressure on the wound is undesirable. The best position for the surgical patient to assume during convalescence is determined individually in each case.

**Maintenance of Body Heat.**—Some elevation of body temperature can be expected in most patients for a day or two after a major operation. During this time, a weakened or febrile patient must be covered and protected from drafts, and wet sheets and bedclothes should be changed as promptly as possible. Frequently, in caring for a patient with lowered general resistance, it may be wise to omit the routine bed bath rather than to subject the individual to the exposure and consequent chilling. Too much covering should always be avoided, especially in hot weather; the excess weight is undesirable and undue sweating may make the patient unnecessarily uncomfortable.

Additional heat may be supplied when needed, as in case of reactions to intravenous medications or in sudden chills, by the use of hot-water bottles wrapped in towels. If the water is used at a temperature of 130 to 140° F. and the bag itself is not allowed to come into contact with the unprotected skin, burns will be avoided. Such burns are common and are usually due to carelessness; the danger should be remembered especially when hot-water bags are placed around an unconscious patient or one who has a nerve lesion with impairment of sensation.

A heat tent may be used to supply warmth to the abdomen when the weight of the bed coverings would be detrimental. It should be large enough to avoid the possibility of the patient's suffering a burn from the light bulbs used to supply the heat. Several bulbs of small size are preferable to one large one since the resultant heat is more evenly diffused and can be more readily adjusted by altering the number of bulbs in use. A thermometer hung within the tent is of service; the temperature should not exceed 90° F. for any long period of time. Such a tent is frequently utilized in the management of paralytic intestinal obstruction, some authorities maintaining that the heat so applied tends to stimulate peristalsis. It should be used with great care when tissue circulation is impaired or regional gangrene is impending; a slight excess of heat locally often speeds the spread of the gangrenous process. The tent alone will prevent pressure upon an area with compromised circulation, but the light bulbs are not to be used. Application of heat to the abdomen by means of a heat tent or diathermy has been suggested as a means of increasing blood supply to the extremities, when the distal circulation is compromised.

**Sedation.**—Postoperative orders for relief of pain are preferably written on the chart in the operating room but may be left on the ward when the patient is brought back. A narcotic is generally ordered, to be administered as soon as the patient begins to regain consciousness, so that he may immediately secure a restful sleep. Morphine sulfate, 10 to 16 mg. (gr.  $\frac{1}{6}$  to  $\frac{1}{4}$ ), hypodermically is usually prescribed (according to the size and age of the adult patient). This drug sometimes produces nausea, vomiting, and general distress. Pantopon, 20 mg. (gr.  $\frac{1}{3}$ ) hypodermically, Schlesinger's solution, 0.3 to 0.7 c.c. (mg. 6 to 10) hypodermically, Dilaudid, 2 to 3 mg. (gr.  $\frac{1}{32}$  to  $\frac{1}{20}$ ) hypodermically, or Demerol, 100 to 200 mg. hypodermically, may be substituted for morphine. Schlesinger's solution is often especially useful in patients who cannot tolerate morphine. The solution is made up so that 0.5 c.c. contains scopolamine hydrobromide, 0.125 mg., morphine hydrochloride, 10 mg., and ethyl morphine hydrochloride, 20 milligrams. The usual dose of 0.5 c.c. is approximately equivalent to morphine, 16 mg. (gr.  $\frac{1}{4}$ ). Whatever drug is given, an amount large enough to secure comfort for the patient should be administered, since undisturbed rest is indispensable at this period.

During the first thirty-six hours opiates are used as frequently as necessary to control postoperative pain. This is especially true at night when a full dose should be given sufficiently early to assure restful sleep. Narcotics are not ordered more often than at three-hour intervals except under unusual circumstances and the respiratory rate must not be permitted to drop below 12 per minute as a result of the depressant effect of the members of the morphine group. Morphine may also predispose to the development of pulmonary complications in debilitated patients because of the accompanying respiratory depression.

The stronger opiates are rarely needed for more than two days following operation and tend to produce habituation if given over too long a period of time. After the immediate need for powerful sedation has passed, a milder drug such as codeine may be employed. If used hypodermically, codeine phosphate, 32 to 64 mg. (gr.  $\frac{1}{2}$  to 1), will prove sufficient; after twelve to twenty-four hours this dose may be halved and may be given by mouth together with aspirin when necessary.

Children require smaller doses of narcotics than do adults and, as a rule, do not need them as often. During the immediate postoperative period, children from 2 to 6 years of age will respond well to codeine phosphate hypodermically, 8 to 16 mg. (gr.  $1/8$  to  $1/4$ ). For younger children a few drops of paregoric by mouth will suffice, and this drug can be used effectively also in quantities of 4 to 8 c.c. (dr. 1 to 2) for patients up to 3 years of age. Children between the ages of 6 and 12 years will require codeine, 8 to 32 mg. (gr.  $1/8$  to  $1/2$ ), or rarely morphine, 4 to 6 mg. (gr.  $1/16$  to  $1/10$ ), depending upon age and weight of the patient. In subjects over 12 years of age, the dose of morphine is apportioned according to weight and maturity of the patient, a dose of 6 to 8 mg. (gr.  $1/10$  to  $1/8$ ) being effective in almost all adolescents, who are usually unaccustomed to such medication and therefore respond to relatively small doses.

An excessively nervous patient at times may clamor for a hypodermic and refuse to be quieted by any other means. If the medication is required because of nervousness rather than pain, sodium phenobarbital may be substituted. A test injection of sterile distilled water or atropine, 0.3 mg. (gr.  $1/200$ ), sometimes also proves the neurotic basis of the request by affording relief. Such practices are psychologically poor and should not be followed. The situation must be explained to the patient and oral doses of the milder sedatives used. If the patient simply has difficulty in sleeping at night during convalescence, a hypnotic drug should be used. Choice of sedative depends on the particular effect desired.

During the first few days after operation pain may often be relieved without the use of drugs by the correction of some small source of discomfort, as by the loosening of a tight dressing, a change of position in bed, the administration of a small enema, or the insertion of a rectal tube for the relief of distention. Sometimes, too, inspection of the patient's incision may reveal the cause of the distress, and removal of a single stitch that is tied too tightly or slight shortening of a drain may relieve the discomfort. At operation, if the skin and retention sutures are placed just tightly enough to secure proper approximation of the wound edges, the patient will suffer less postoperative pain in his incision and will be less likely to develop a wound infection or an unsightly scar. Some degree of edema always develops



in the wound during the immediate postoperative period, and snug sutures will usually become tighter and cut into the skin.

Application of one or two ice bags without covering to the dressing will sometimes relieve pain in the incision as effectively as an analgesic drug. This is particularly true if the dressings over the wound are light rather than bulky.

**Nausea.**—Nausea and vomiting are the usual sequelae of almost every general anesthetic, the severity of the reaction depending upon the condition of the patient and the type and duration of the operation and anesthesia. In the average uncomplicated case these symptoms disappear when the anesthetic has been totally eliminated and require little attention beyond ordinary nursing care and the availability of an attendant. When nausea is prolonged, an infusion (1,000 c.c.) of dextrose, 5 per cent, in distilled water is usually helpful; persistent nausea often responds also to the hypodermic administration either of antispasmodic drugs such as papaverine, 30 mg. (gr.  $\frac{1}{2}$ ), or atropine, 0.5 mg (gr.  $\frac{1}{120}$ ), or of hypnotics such as sodium phenobarbital, 0.13 Gm. (gr. 2). The tendency of narcotic drugs to produce nausea should be remembered.

As soon as nausea has ceased, the patient is given mouthfuls of tap water as desired, preferably either hot or chilled rather than at room temperature. In general, small sips of water or bits of cracked ice offer no advantage since the patient is much more likely to swallow quantities of air, which contribute to the development of postoperative distention.

**Prevention of Complications.**—During the early period of recovery, complications must be watched for and detected as soon as possible. Shock and hemorrhage are among the most serious of these, and postoperative nursing care is devoted largely to proper prophylaxis. Too much emphasis cannot be given to the necessity for control of the factors which predispose to these states. In this respect, chilling, pain, undue disturbance, and slight but continued bleeding are most important, and neglect of such conditions will often transform incipient shock into fully developed collapse. The intravenous administration of blood transfusions or other fluids as indicated constitutes an exceedingly valuable preventive measure which should never be neglected when shock is threatened.

In older and more weakened patients, and especially in those with heart disease, pulmonary complications are likely to develop as a result of improper aeration of the lungs. Such complications should be anticipated and usually can be prevented by early institution of exercises in bed and by administration of a mixture of carbon dioxide and oxygen at frequent intervals during the first twenty-four hours after operation (p. 366). Some surgeons advocate early ambulation for prevention of postoperative pulmonary complications; others who use carbon dioxide for a respiratory stimulant prefer to use the pure gas rather than a mixture with oxygen (p. 367). The usual procedure, however, is to employ the gaseous mixture, regulated to contain from 5 to 10 per cent of carbon dioxide and administered every one to two hours for the first day. The gases are given most satisfactorily through a mask, if one is not available, an intranasal catheter will suffice. Inhalations are given until the patient takes several deep breaths involuntarily as a result of the stimulation, but he should not be forced to pant violently as a result of inspiring too much carbon dioxide or too concentrated a mixture. The gas also may be given at the proper intervals to a patient receiving oxygen intranasally by connecting a tank of carbon dioxide to the end of the nasal catheter with a Y tube, so that oxygen and carbon dioxide can be administered simultaneously. It is preferable to introduce small amounts of carbon dioxide at stated intervals rather than to employ a constant low percentage of the gas, because the latter, administered in such a way, has little stimulating effect on respiration and is toxic.

If an anesthetic apparatus is not available, a paper bag may be substituted as a rebreathing chamber, so that the respirations are stimulated by the patient's own carbon dioxide, or an attendant may direct him, at intervals of thirty to sixty minutes, to take a dozen deep breaths. Attention to this measure may help to prevent postoperative pulmonary complications in many cases.

It is sometimes necessary to order the administration of oxygen immediately after operation (p. 804), particularly in patients with impending shock or with pre-existing cardiac or pulmonary disease or hyperthyroidism. Use of oxygen should never be delayed until the need for it becomes obvious; it is

much more useful as a preventive measure in surgical patients than as a therapeutic measure. Clinical cyanosis may not appear in an anemic patient until after irreversible tissue damage has been caused by prolonged anoxemia; the optimum time to begin oxygen therapy is just before it becomes necessary.

**Fluid Balance.**—The surgical patient loses a moderately large amount of fluid in the operating room, the quantity lost depending chiefly on the temperature and humidity of the operating suite and on the operative procedure. Loss of fluid through bleeding is generally greater than it appears to be (p. 160). Insensible evaporation and sweating are both greater than normal and may be responsible for the loss of from 1 to 3 liters of fluid during the course of a long operation. The patient returns from the operating room with a fluid deficit already established and with a tendency to lose more than the normal amount by evaporation because of the invariable postoperative rise in body temperature.

If postanesthetic nausea is mild and of short duration, the average good-risk patient can be permitted to pass the first day after operation with a slight fluid deficit. The quantity of fluids taken during the next twenty-four hours must be watched closely to make sure that an adequate intake is maintained. During this period cool or chilled water is preferable to ice water, because it is easier to drink. Relatively small quantities administered at frequent intervals are taken more readily than large amounts drunk at once. During this time other drinks may be added according to the patient's tastes, with the exception of milk, which curdles into a solid mass when it reaches the stomach and also tends to produce intestinal distention. If the patient expresses a desire for soft drinks such as ginger ale or Coca-Cola, these may be given in small quantities. If oral fluid administration is properly planned and if quantities taken are carefully recorded during the immediate postoperative period, the average patient not suffering from prolonged nausea can be persuaded to take sufficient fluids by mouth.

Following more severe operations and during the hot summer months, fluid loss is even greater and the patient shows evidence of a more marked postoperative reaction. Under

these circumstances, if nausea persists and the patient cannot take sufficient fluids orally, evidences of dehydration and acidosis may appear. The pulse rate becomes much more rapid and the pulse pressure drops, the respiratory rate and temperature may rise, and the lips and tongue become dry and parched. If the deficiency is allowed to persist, the patient soon becomes restless and irritable and complains bitterly of thirst, although unable to drink because of nausea. As acidosis develops, acetone and diacetic acid may appear in the urine and the quantity of urine diminishes, the specific gravity rising concomitantly.

As stated elsewhere, fluid intake must be sufficient to permit a daily urine output of 600 c.c. minimally, which must be concentrated to a specific gravity of 1.030 in order to carry off the solid end products of metabolism. If less urine is excreted, retention of waste products occurs, as evidenced by the increased blood nonprotein nitrogen. Since fluid loss by exhalation, insensible evaporation, and sweating is immediately necessary for proper heat regulation, a decrease in urinary output is an immediate and dependable guide to the amount of fluid required for replacement. A twenty-four hour urinary excretion of 1,000 c.c. is acceptable, but 1,500 c.c. is probably the optimum amount. In the computation of the proper daily total for fluid intake, every source of fluid loss must be recognized and the amount lost estimated as accurately as possible. Part of this duty devolves upon the nurse in attendance, who must be thoroughly impressed with the necessity of recording each measurable quantity of vomitus, urine, or drainage material on one side of the chart and all amounts of fluid given by mouth, per rectum, or parenterally on the other.

In a typical case, one day's total output may have been measured as 900 c.c., consisting of 700 c.c. of urine and 200 c.c. of stomach contents. Insensible loss by evaporation may have approximated 1,500 c.c. during the twenty-four hours, amounting to 40 per cent of the total fluid loss<sup>3</sup> and depending upon the size of the patient rather than upon the operative procedure. Loss by sweating may have amounted to 400 c.c., depending largely on the season and the atmospheric conditions. Added to that would be the amount carried in the exhaled air, possibly 300 cubic centimeters. These losses would total 3,100 cubic centimeters. However, since the urinary output is noted to be

insufficient, replacement of this total amount of fluid would not maintain a proper fluid balance; an additional 800 c.c. would have to be given in order to reach the optimum state. A total of 3,900 c.c. would therefore be administered to this particular patient on the following day, as much by mouth as possible and the remainder according to the preferences of the attending surgeon. If the weather changed or the patient's fever increased, fluid loss by evaporation would change proportionately and would be reflected by alterations in the urinary output.

No set quantity of fluid can be established, therefore, as the proper fixed quantity for administration after operation. At times much too little is given because of inattention, improper charting, or lack of appreciation of the fundamental facts concerned. At other times serious waterlogging may develop as a result of too enthusiastic and ill-advised forcing of large quantities of fluids. This is especially dangerous in patients with associated cardiac, renal, or pulmonary disease, particularly when too much salt solution is used, with resulting water retention. In each case a critical estimate should be made each day of the total fluid loss and of the total fluid required during the next twenty-four hours, checked by the amount of urine output (Chapter 2).

**Diet.**—The dietary plan during the postoperative period should be as nearly as possible a continuation of the principles and practices governing the preoperative dietary preparation. Before operation carbohydrates and fluids are forced in order to supply a reserve for the day of operation and for the subsequent period during which the patient is unable to take food by mouth. In accordance, the intravenous fluids furnished after operation to the nauseated surgical patient carry a relatively large amount of dextrose. Full diet should be restored as rapidly as possible to prevent exhaustion of the body carbohydrate stores with resultant acidosis.

During the immediate period of nausea no food and little fluid can be swallowed. Dependence at this time is placed entirely on nutrition given parenterally, even water by mouth being withheld until the period of marked nausea has passed. During the first twenty-four to forty-eight hours after operation, a strictly liquid diet will prove most satisfactory and usually

consists of water, ginger ale, hot tea, and hot broth, but not including such liquids as milk and cocoa, which solidify upon reaching the stomach and are normally retained in the stomach for a relatively long period. Fruit juices, particularly canned fruit juices, are not taken well during the period of recovery from postoperative nausea, perhaps because of their high sugar content. A little later, thin soups may be added to the diet. When the patient is taking liquids of this type with enjoyment, solid foods may be offered, usually within two to three days after operation. Occasionally a patient who continues to be nauseated without apparent reason actually may be hungry without realizing it; in such a case, a bit of dry toast and a thin slice of cold roast beef or chicken may dissipate the nausea promptly.

Persistent nausea often responds readily to intravenous administration of dextrose. It must be remembered that even though the liver glycogen has been pushed to as high a level as possible, the total carbohydrate available from this source is still not over 5 per cent of the total weight of the liver. Since the average liver weighs about 1,500 grams, this amounts to little more than 75 Gm. of available dextrose, which is capable of supplying only about 300 calories. It is apparent, therefore, that supplementary carbohydrate must be supplied soon after operation.

A moderate degree of starvation is to be expected during the first few days after operation, when the food intake is so sharply restricted. Normal requirements for a healthy adult approximate 1 calorie per kilogram per hour (about 1,600 calories for an adult weighing 65 kilograms) and the basal metabolic rate rises about 7 per cent for each 1° F. of fever, increasing the caloric need.

A daily minimum of 1,600 calories is difficult to give by parenteral routes alone, since 100 Gm. of protein hydrolysate and 100 Gm. of dextrose is the maximum that can be administered conveniently (p. 76). This quantity of protein and carbohydrate will supply about 800 calories. When no food is supplied from exogenous sources, body fat and carbohydrate are utilized to supply energy, starvation acidosis (ketosis) developing when the available carbohydrate drops below a minimum level. Since the supply of stored carbohydrate available for

calorigenic use is soon exhausted, body protein is broken down to form glucose for metabolism in conjunction with the stored fat. As a rule, 100 Gm. of carbohydrate daily will suffice to maintain a proper balance between oxidation of fat and carbohydrate and thus to prevent development of ketosis.

Therefore, if the patient is unable to take food by mouth during the first few days after operation, at least 100 Gm. of dextrose should be given intravenously daily and a close check kept on the urine for the appearance of acetone or diacetic acid. If any evidence of acidosis appears, reflected either in the urine or in the blood carbon-dioxide combining power, the amount of parenteral carbohydrate given must be increased. Appropriate quantities of protein hydrolysate given parenterally will be of value in such cases.

After disappearance of nausea, broths and soups offer the next step in expanding the average postoperative diet. On the third day a soft diet low in fat can usually be started and may be given sooner if the patient can take it, except, of course, after gastrointestinal operations. At this time milk and milk products such as ice cream may be added to the diet list, in small amounts at first. Resumption of the normal diet depends entirely on the patient's ability to eat. When dietary changes are made, portions should be relatively small and the tray should present as inviting an appearance as possible. The average individual has little appetite for several days and he may find himself actually repelled by the sight of a tray filled with large quantities of food.

Special procedures and special complicating conditions may require specific dietary procedures. These are discussed in appropriate sections and a list of typical foods to be included in each type of diet will be found in the Appendix.

**Elimination.**—Intestinal peristalsis slows down even in a normal individual when he is confined to bed and regular bowel movements are not to be expected in a patient following an operation. No cathartics, however, are given for several days after an ordinary surgical procedure. Except in case of operations upon the gastrointestinal tract, mild cathartics generally may be employed when there is evidence of returning peristalsis following operation. Drastic catharsis is likely to

cause the loss of quantities of fluid, and frequent bowel movements tend to weaken the individual.

As a rule, abdominal distention, gas pains, and constipation are best treated by means of small enemas and frequent insertions of a rectal tube for the first few days. An enema consisting of two ounces of water and two ounces of glycerine acts as a low rectal irritant and usually produces the desired result. In more intractable cases of distention specific measures may be necessary (p. 324).

The large soapsuds or tap water enema is not used during the first two or three days following operation, chiefly because of the effort required in expelling it. After the patient has regained strength, this treatment may be used in preference to cathartics, which sometimes fail. Inasmuch as old, chronically ill, or nervous patients have a strong tendency to become constipated, special attention should be paid to this consideration when night orders are left. An adequate fluid intake, aided by mineral oil or a mild laxative such as aromatic cascara usually will assure proper elimination. Long-continued use of enemas can create a bowel habit which makes the person dependent on them for regular evacuations. This should be explained to the patient and avoided by the substitution of other measures.

Occasionally, fecal impaction will be discovered before operation or will develop in a convalescent patient whose bowel movements are too infrequent. It may be relieved by administration of a retention enema of six ounces of cottonseed oil or olive oil at night and a hot (110° F.) soapsuds enema in the morning, with or without two ounces of peroxide added. Proper daily attention to the record of bowel movements will prevent the development of this complication.

Postoperative diarrhea may occur at times and may be controlled by administration of paregoric, 8 c.c. (dr. 2), repeated if necessary. In less responsive cases flushing of the colon with a tap water enema will usually remove the offending irritant.

**Getting Up.**—During the first day or two after operation, the sutured wound is strong and in good physiologic condition. From the second to the fifth day, edema develops, the sutures become relatively tighter, and vascular congestion appears. The formation of granulation tissue between the apposed surfaces of the incision progresses from the day of operation to the fifth



day, when fibrosis and contraction begin, causing shrinkage and transformation of the soft granulations into firm fibrous scar. The period during which the healing incision is weakest is from the fourth to the eighth days after operation, when edema and vascularity are at their peak. This is called the lag period of healing and is followed by a period of fibrosis (eighth to fourteenth days), during which the incision healing by primary union increases rapidly in strength. Union of the wound is complete within two weeks after operation, the scar slowly shrinking and becoming less vascular over the ensuing months.

There are two widely different opinions concerning the time at which a surgical patient should be allowed up after operation.

The older and still more generally accepted point of view is that the convalescing surgical patient should be kept in bed for from twelve to fourteen days, until the lag period of healing is over and firm fibrous union has occurred in the scar. The particular time of arising, however, depends upon the patient's condition, the type of operation, the presence of complicating factors, and the location of the incision. A healthy patient who has had a smooth convalescence following a gridiron or McBurney incision may be allowed up after five or six days. Little tension is placed on this type of incision by muscular exertion, since the muscle fibers and lines of separation are in different directions and there is no tendency for the incision to gape on muscular contraction. Following an incision which splits the fascial and muscular layers, such as a midrectus or a paramedian incision, there may be some impairment of muscle innervation. In this type of incision the lines of division in each layer are nearer the midline of the abdomen and are almost superimposed, so that much more tension is placed on a defect potentially weaker than the gridiron type of wound. Patients who have had incisions through or across the rectus muscle are kept in bed for from twelve to fourteen days, depending upon the rapidity of convalescence. If drains are carried through the incision itself or if any wound complication develops, the defect usually is allowed two or three more days to heal before much tension is placed upon it. A large drainage tract, especially if continued infection is present, may prolong convalescence for several weeks. The same procedure is followed in case of lower midline or hernio-

plasty incisions, which usually heal sufficiently in twelve days to permit the patient to get up. In all cases, however, regular active exercises of the arms and legs and frequent changes of position are mandatory, beginning on the day of operation.

More recently, considerable attention has been directed to the rationale of early rising and early ambulation following operation. This practice, which has been more or less routine in Europe for many years, has been tried and advocated with much enthusiasm lately by many surgeons. Although first advocated as long ago as 1899, early rising after operation was not practiced extensively in this country until 1941, when such excellent results were reported in several series of cases<sup>3, 4</sup> that interest became widespread. The procedure usually followed, in addition to the usual routine measures of postoperative care, is to help the patient get up and stand beside the bed on the morning after operation and to take a few steps either that day or the day following. Ambulation then is attained rapidly and the patient walks about unassisted and as desired after the fifth day. Use of an abdominal binder is advisable. If, on the first occasion, the patient rolls to the right side, puts his feet out of the bed, and then is helped to sit up, the discomfort experienced on arising will not be too extreme. Change of position can be aided by elevation of the upper half of the bed as the patient sits up. The patient is requested to breathe deeply and to cough, while supporting the incision by manual pressure, the first few times he is up.

The rationale of early ambulation is stated to be that prompt exercise stimulates respiration and cardiovascular function and increases the blood supply to the operative area while the holding power of the sutures is still at a maximum. Increased blood flow and increased oxygen supply promote more rapid healing, shorten the lag period, and actually decrease the likelihood of wound complications. It is further claimed that reduction of reflexes arising in the traumatized area permits normal respiratory activity of the diaphragm, with consequent rapid return to normal of pulmonary ventilation and vital capacity. Decrease in incidence of pulmonary complications therefore may be expected. No increase in wound dehiscence or in the development of postoperative hernias has been noted. All current reports on the subject agree that the morale of the patient is improved,

less nursing care is necessary, convalescence is more rapid, strength returns more quickly, and the patients are well pleased after the first uncomfortable day or two have passed and confidence is gained. Not even the most enthusiastic advocates of early ambulation suggest its use in all patients, however; patients who have cardiac disease, acute pulmonary disease, hepatitis, peritonitis, or *pancreatitis*, patients recovering from shock or severe hemorrhage, patients who have clinical thrombophlebitis, and patients with medical, orthopedic, or neurosurgical conditions requiring bed rest are not to be allowed up until their general condition warrants it. Patients who are kept in bed or who refuse to get up during the first forty-eight hours after operation should be kept in bed for a full ten to fourteen days, since the success of early ambulation depends upon increased blood supply and increased healing in the fresh wound while the sutures offer maximum support. The patient is also cautioned not to sit in a chair during his first few days of ambulation but to return to bed when tired, since pressure of a chair against the lower thighs and upper legs may encourage venous thrombosis at this time. While advocates<sup>6</sup> of early ambulation are increasing and convincing reports of use of the procedure continue to appear, most surgeons still employ the older plan of rest in bed until healing of the incision has occurred.

Any metabolic or deficiency disease will decrease the rapidity and strength of the repair process; steps must be taken to supply the lacking factors. Anemia and hypotension may retard wound healing by keeping the actively growing tissue in a state of relative anoxia; vitamin deficiencies apparently result in a weakened union. Vitamin C, which has received particular attention in this respect, is thought to be concerned with the intercellular cement substances and the formation of fibrous tissue; cevitamic acid in proper doses may minimize the development of wound complications based on sluggish and weak repair.<sup>6,7</sup> Since asymptomatic scurvy is not uncommon, its probable effects on wound healing must be remembered and the deficiency corrected. The diagnosis of avitaminosis C may be substantiated by tests for plasma content of ascorbic acid. It has also been found<sup>8</sup> that a high protein diet will increase both the speed and strength of wound repair, while a high fat and low protein diet will produce the opposite effect.

Although the subject of choice of suture materials is a highly controversial one, it is usually agreed that patients whose incisions are repaired with nonabsorbable materials such as silk or cotton may be allowed up sooner than those whose wounds are closed with catgut, provided that no wound complication has occurred.

**Encouragement.**—Mention must again be made of the fact that the average surgical patient, no matter how calm and well poised in daily life, is a stranger in a most unfamiliar environment, his very existence in the hands of individuals with whom he is not even well acquainted, as a rule. Consequently, the demeanor and attitude of those around him, to whom the care of patients is a daily routine, play a great part in his sense of security and faith in the ultimate outcome of treatment. An artificial bedside manner and an oversympathetic attitude are to be deplored, but simple matter-of-fact interest and ordinary friendliness will put an apprehensive individual at ease and will convince him that the doctors and nurses are interested in him as a person and in his recovery rather than as a specimen or as a case number.

### References

1. Spalding, J. E., and Lond, M. S.: Fowler's Position, *Lancet* 250: 643, 1946.
2. Fuge, W. W., and Hogg, B. M.: Insensible Loss in Surgical Patients, *Ann. Surg.* 108: 1, 1938.
3. Leithauser, D. J., and Bergo, H. L.: Early Rising and Ambulatory Activity After Operation; Means of Preventing Complications, *Arch. Surg.* 42: 1086, 1941.
4. Leithauser, D. J.: Confinement to Bed for Only 24 Hours After Operation; Means of Preventing Pulmonary and Circulatory Complications and of Shortening Period of Convalescence, *Arch. Surg.* 47: 203, 1943.
5. Schafer, P. W., and Dragstedt, L. R.: "Early Rising," Following Major Surgical Operations, *Surg., Gynec. & Obst.* 81: 93, 1945.
6. Wolfer, J. A., Farmer, J., Carroll, W. W., and Manshardt, D. O.: An Experimental Study in Wound Healing in Vitamin C-Depleted Human Subjects, *Surg., Gynec. & Obst.* 84: 1, 1947.
7. Taffel, M., and Harvey, S. C.: Effect of Absolute and Partial Vitamin C Deficiency on Healing of Wounds, *Proc. Soc. Exper. Biol. & Med.* 38: 518, 1938.
8. Ravdin, I. S., Stengel, A., Jr., and Prushankin, M.: The Control of Hypoproteinemia in Surgical Patients, *J. A. M. A.* 111: 107, 1940.

## CHAPTER 7

### SHOCK

Peripheral circulatory failure is a condition well known to every doctor, no matter what type of medicine he practices. Those who deal with the branches of internal medicine see the manifestations of it in patients suffering from toxemia, overwhelming infections, anaphylaxis, severe dehydration, hyperinsulinism, and similar states. Physicians who interest themselves in the surgical fields see progressive circulatory failure in patients who have sustained severe trauma, extensive hemorrhage, loss of plasma, or a combination of these. The clinical picture of shock due to any of these factors is much the same, the patient exhibiting falling blood pressure, rising pulse rate, extreme weakness, and coldness and pallor of the skin. Some impression must be reached as to the cause of the symptoms, since proper treatment may depend upon the causative factor. Patients with surgical shock, however, respond well to transfusions of blood, whether the condition is due to hemorrhage, plasma loss, or severe trauma.

Much investigative work, both experimental and clinical, has been done since World War I to discover the physiologic basis for shock and to establish the most effective methods of treatment. A great deal more information has been added by studies carried on at the battlefronts of World War II, where shock and hemorrhage were all too common. Despite these studies, the pathogenesis of shock is still somewhat uncertain and there is still some discussion concerning the best and most effective methods of treatment. Shock probably is due to several causative factors rather than to any single one. Conditions in the laboratory, where shock may be produced experimentally by single causative agents, do not commonly occur in ordinary life.

Although there is disagreement concerning theories of origin, it is universally accepted that the manifestations of shock depend chiefly on a reduction of the circulating blood volume, either by loss of plasma or blood or both, to a point at which actual circulatory failure and generalized tissue anoxia occur. There is no

relation, of course, between the circulatory collapse of shock and that of advanced heart disease. In shock, the vascular disturbance is characterized by and is due to peripheral failure, while in cardiac failure the primary fault is in the heart itself. Diminished cardiac output in shock is dependent on a lowered venous pressure, which results in a decreased return of blood to the right auricle; lowered cardiac output in heart failure is due to a primary insufficiency of the heart, which is accompanied by an increased venous pressure. The myocardium in severe shock may suffer from anoxemia and in this way may also become a factor in decreasing the volume of blood delivered to the aorta.

### Pathogenesis

The clinical picture of shock may vary according to the causative factors involved, but the pathogenesis is based primarily on the presence and physiologic effects of peripheral circulatory failure. Shock can be divided broadly into two main types, primary or immediate, and secondary or delayed.

**Primary Shock** may follow some sudden severe trauma and is immediate in onset. It is seen frequently also following anesthesia (particularly spinal) and after operations, especially on the upper gastrointestinal tract or the central nervous system. Primary shock, so called, is nothing more than a reflex vasodilatation in response to nervous overstimulation. There is a sudden drop in blood pressure as a result of the increased capacity of the vascular bed, and the pulse becomes feeble and soft, with perhaps some increase in rate. The coldness and pallor of the skin probably are due to an associated peripheral reflex vasoconstriction which develops to compensate for the sudden decrease in circulating volume of the blood. With the generally decreased pressure, the return flow of blood to the heart diminishes rapidly, cardiac output drops, pulse rate rises, and the clinical signs of shock appear. There is no change in the total quantity and no significant alteration in the proportion of each blood component. The circulating volume simply is suddenly reduced by the impounding of quantities of blood in the smaller vessels throughout the body.

Primary shock is not really shock at all but is more properly called syncope. It is identical with the "faint" of a person who

receives a sudden psychic shock or who overexerts in the presence of hypotension. In the absence of severe injury or blood loss, the symptoms disappear and the blood pressure returns to normal if the patient is placed in a recumbent position and stimulants are given. When associated trauma is present, secondary shock may follow as a result of the injury or blood loss and merge into the period of recovery from primary shock, so that the shock-like state develops immediately upon injury and persists, growing deeper and more profound as time passes.

**Secondary Shock.**—The clinical symptoms of secondary shock due to trauma and to conditions causing obvious loss of plasma (for example, burns) are much the same as those due to hemorrhage. The physiologic changes may be somewhat different, however, and the effects of shock and of severe hemorrhage sometimes can be differentiated.

Since there are many different causes for shock, the physiology, clinical picture, and preferred treatment may vary in details although they are fundamentally the same. It is probably better, as Blalock<sup>1</sup> has suggested, to use a descriptive phrase and speak of shock due to trauma, shock due to burns, or shock due to hemorrhage.

The facts that shock may vary in nature and may be due to different causative factors, with somewhat different physiologic responses, probably are responsible, at least in part, for the many theoretic explanations that have been offered. Primary shock was produced in experimental animals in 1863 by Goltz, who ascribed the condition to reflex vasodilatation. Crile, after considerable experimental and clinical observation, concluded that shock is on a neurogenic basis and results from exhaustion of the vasomotor centers following overstimulation. He amplified this view by stating that certain factors such as worry, fear, and emotional tension contribute to the development of shock, particularly of the postoperative type. He therefore advocated reduction of operative injury to a minimum and careful attention to the avoidance of any psychic trauma to the patient.

While psychogenic factors and stimulation of nervous tissues at operation are not the only factors involved in postoperative shock, they are of contributory importance. Much improvement in postoperative results has followed general adoption of the precautionary principles advocated by Crile and his followers.

Other theories that have been proposed to explain the physiology of shock include acapnia, fat embolism, acidosis, hyperactivity of the adrenal medulla, exhaustion of the adrenal medulla, and adrenal cortical insufficiency. In some cases one or more of these factors may produce a shocklike picture, but none is generally accepted as the underlying physiologic background for shock.

Studies on the nature of shock were stimulated by World War I during which Keith demonstrated a reduction of circulating blood volume in shock occurring in wounded soldiers. He showed also that the severity of the shock is directly proportionate to the decrease in blood volume and that hemoconcentration may be present, indicating loss of plasma rather than of whole blood. On the basis of other experimental work and observations on wounded men during this time, the theory of traumatic toxemia was developed to explain the physiology of shock. Much of this work was done by Cannon,<sup>2</sup> who explains this theory as follows:

"The theory of secondary shock which has the strongest support, both in clinical observations and in laboratory experiments, is that of a toxic factor, arising from damaged and dying tissue and operating to cause an increased permeability of the capillary walls and a consequent reduction of blood volume by escape of plasma into the lymph spaces . . . . It is recognized that after a sufficient time infection may occur and be of such character in itself as to induce a persistent low blood pressure. According to this theory there might be no essential difference between the effects of toxins given off by damaged tissue and of toxins resulting from activity of bacteria."

Cannon and his followers, therefore, maintain that secondary shock of traumatic origin is due to the effects of a toxin formed at and absorbed from the damaged area, the degree of shock often being out of proportion to the size of the area involved. The hypothetical toxic vasotropic substance is thought to act in a manner somewhat similar to histamine, producing a generalized capillary dilatation with a resulting drop in blood pressure and increased capillary permeability, followed by transudation of



fluid into the tissues. There is a consequent actual decrease in the circulating and the total blood volumes. Despite many clinical and experimental investigations, no one has yet been able to demonstrate a histamine-like substance either in the blood stream of a shocked patient or in tissue extracts from the traumatized area, perhaps because, as suggested by Moon,<sup>3</sup> chemical methods of identifying such substances except as nonprotein nitrogen have not yet been perfected.

Repetition of Cannon's experiments by others (Parsons and Phemister<sup>4</sup> and Blalock<sup>5</sup>) did not result in confirmation of Cannon's findings. These investigators agreed that experimental trauma to an animal's limb produced a swelling and an increase in weight in the limb. They found, however, that the weight gain indicated that fluid amounting to approximately one-half of the total blood volume was lost into the traumatized area, which was sufficient in itself to account for the fall in blood pressure. Cross transfusion of blood from shocked animals to normal animals produced no drop in blood pressure, from which the authors concluded that shock was due solely to fluid loss into the traumatized area, whether of plasma with hemoconcentration resulting, or of blood, either with no blood change or with hemodilution resulting, and that no evidence of a toxic substance was found.

Advocates of this theory (hematogenic) state that loss of fluid from the blood stream is partially compensated by generalized vasoconstriction, the blood pressure and pulse rate thus being maintained near the normal levels. Under these circumstances, when the venous blood returned to the heart is diminished too greatly, the blood pressure falls progressively. Later, vasodilatation occurs as the terminal stage of shock approaches and the blood pressure sinks to an undeterminable level. At this point the effects of anoxia appear, with acidosis, hypometabolism, anuria, and all the other typical features of secondary shock. If the lost blood or plasma is not soon replaced, toxic metabolic substances develop, generalized capillary permeability appears, and the shock is said to be irreversible, with death soon occurring in spite of transfusions at this stage.

At the beginning of World War II, there were in general, therefore, three main hypotheses to explain the pathogenesis of shock:

1. *Hematogenic*.—Decreased total blood volume resulting from loss of large quantities of plasma, of blood, or of both into or from the traumatized area (Blalock, Phemister, and others).

2. *Vasogenic or Toxigenic*.—Formation of a histamine-like toxin at the site of trauma, with generalized increase in capillary permeability and transudation of plasma into the tissues of the body following absorption of the toxin into the systemic circulation (Cannon, Moon, and others).

3. *Neurogenic*.—Generalized vasodilatation due to excess stimulation of the vasomotor center (Crile and others). This theory refers at the present time chiefly to primary shock.

Proponents of each theory agree on the facts that plasma loss and blood loss will produce shock; the points of disagreement center chiefly on the site of fluid loss and the reason for its loss.

In general, the physiologic changes seen in shock may be summarized as follows: loss of fluid from the circulating blood reduces the circulating blood volume and consequently reduces the venous return to the heart. The cardiac output is correspondingly decreased but for a time is compensated by reflex peripheral vasoconstriction, which maintains the blood pressure at a relatively normal level. When fluid loss increases still further or when compensatory vasoconstriction fails, the blood pressure drops and the blood supply to the body tissues is decreased. Tissue anoxia results, with depression of all visceral functions, especially in the liver, kidneys, and brain. Prolonged tissue anoxia terminates in irreversible shock, with generalized vasodilatation, pooling of blood in the small vessels, fall in blood pressure below the level at which life can be sustained, and death. It is probable also that prolonged tissue anoxia increases the permeability of the capillary walls, which increases the loss of fluid into the tissues, further decreasing the blood volume. The "vicious circle" of shock can be summarized in a descriptive diagram<sup>6</sup> (Fig. 9).

Further work, done during and after World War II, has been especially valuable because of the large number of clinical cases that were available for study. During the African and Sicilian campaigns in 1943, it was the universal experience of surgeons in the forward hospitals that patients in shock often responded unsatisfactorily to transfusions of plasma and that whole blood

was needed for treatment. This finding, while somewhat disappointing to the high hopes that had been held for dried plasma, corroborated the belief of those who maintain that whole blood rather than plasma is lost at the site of injury in traumatic shock. Later in the war, refrigerated blood was made available in almost any quantities desired in the field and evacuation hospitals, and the response of shocked patients was correspondingly improved. While plasma became of secondary im-

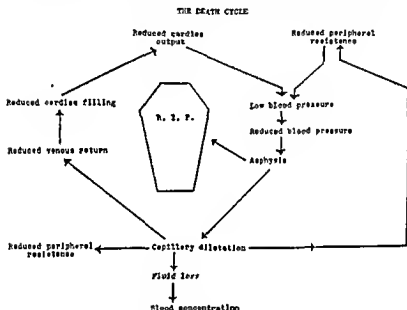


FIG. 9.—The death cycle in shock. (Modified from McDowall. Brit. M. J. 1: 810, 1940, Prof. McDowall's modification.)

portance to blood at these hospitals, it was still the only fluid available for transfusion at the aid stations and collecting stations where there were no facilities for the use of whole blood. Plasma served well to maintain blood pressure at a satisfactory level in shocked patients during their transportation from these points to a hospital station.

Emerson and Ebert,<sup>7</sup> studying severely wounded soldiers treated in field hospitals in France and Germany during World War II, concluded that traumatic shock is essentially a reflection

of diminished blood volume due to loss of whole blood, the loss averaging 40 per cent of the blood volume in severely shocked patients. While plasma transfusions were useful to sustain the blood pressure until whole blood was available, administration of more than the minimum amount of plasma necessary for this purpose caused hemodilution with anemia, allowed further bleeding to occur, and limited the amount of blood possible to transfuse later without overloading the circulation. Transfusion of whole blood, sufficient in amount only to bring the arterial blood pressure to a safe level, was found to be the best method of preoperative therapy. Emerson and Ebert found that the degree of blood deficiency could be estimated best by the level of the arterial blood pressure on admission and by the character and extent of the wounds.

A similar investigation was carried out by Evans and associates<sup>8</sup> during the preceding year. These workers, studying blood volume changes in traumatic shock, found that a loss of at least 15 per cent of the blood volume had occurred in their patients who exhibited shock and that most of the patients suffering from severe shock had lost, on an average, 35 per cent of their blood volume. Evans states that there is little or no evidence of hemoconcentration in patients seen early in shock and that therefore whole blood rather than plasma probably is lost from the blood stream following severe trauma.

**Postoperative Shock.**—The postoperative type of shock is the result of several contributory factors. It is partly due to neurogenic causes as the result of tension upon the abdominal viscera and stimulation of the visceral nerves, partly due to the anesthetic agent used, partly due to the debilitating influence of the disease itself, partly due to emotional and psychic factors, and, in great measure, due to loss of blood and fluid during the operation. Following depletion of the blood volume, the patient's blood pressure is maintained near a normal level for a time by reflex compensatory vasoconstriction. In this "pre shock" state, although the blood pressure and pulse rate may be almost normal, even a relatively slight trauma or metabolic upset may precipitate fully developed shock because of the decreased circulatory reserve.

**The "Crush Syndrome."**—One aspect of shock which has received considerable attention recently is the reaction of the kidneys to various etiologic factors producing shock. It has long been recognized that shock following loss of blood or plasma may be accompanied by oliguria or even anuria, probably as a result of decreased blood pressure in the renal vessels. In such cases, treatment by blood transfusion restores kidney function along with other visceral functions unless shock has persisted so long that it has become irreversible and fatal.

Reports appearing during World War II, however, described a new finding in patients who developed shock several hours after sustaining crushing or compression injuries to skeletal muscles. In many such cases, edema of the injured extremity soon appeared and was accompanied by progressive oliguria or even anuria. Examination of the urine in these patients and also in patients with similar injuries not severe enough to cause shock revealed the presence of relatively large amounts of myohemoglobin,<sup>9</sup> often sufficient to redden the urine. Progressive oliguria in these patients was followed either by slow recovery of kidney function to normal within a period of months or by anuria and death within several days. Post-mortem studies of the kidneys<sup>10</sup> revealed toxic degeneration or cloudy swelling in the proximal tubular epithelium and severe damage and even necrosis in the distal tubular epithelium, with pigment and casts in the distal tubules. The renal changes appear to be similar to those noted following fatal hemolytic reactions to transfusion of incompatible blood, and the clinical symptoms of the two conditions also have much in common.

With the assumption that the crush syndrome might be due simply to local leakage of blood or plasma, Patey and Robertson<sup>11</sup> treated several patients with this syndrome by application of intermittent positive pressure to the injured area continuously for some hours, in addition to the usual measures. A large blood pressure cuff, connected to a Pavex motor for intermittent compression was used, supplying up to 60 mm. Hg pressure. These observers reported successful results in delaying and even in forestalling the appearance of shock in several such cases. Corcoran and Page,<sup>12</sup> following experimental work, suggested that post-traumatic anuria (crush syndrome) may be due to a vasoconstrictor substance liberated from the injured tissues and carried

to the kidneys by the circulating blood. According to this view, vasoconstrictive renal ischemia produces oliguria, and absorption of acid metabolites from the injured muscle produces aciduria. Precipitation of myohemoglobin results, with formation of pigment casts in the renal tubules. Injury to the epithelium of the distal convoluted tubules by ischemia and by a hypothetical nephrotoxin may add to the damage caused by the precipitated pigment. Others<sup>12</sup> have suggested that the renal cortical ischemia of crush syndrome may be due rather to stimulation of the renal vasomotor nerves, with decreased flow to the renal cortex. A discussion of the renal lesions in post-traumatic anuria can be found in the report by Lucké.<sup>14</sup>

Treatment of post-traumatic anuria is preventive; as in the case of hemolytic transfusion reactions, therapy is of little use after the kidney damage has occurred. Proper therapy of any crushing or compression injury of skeletal muscle should include immediate transfusion of blood or plasma, prompt application of an elastic pressure bandage (not a tourniquet) to the entire injured limb snugly but not tight enough to obstruct the blood flow, and administration of sodium lactate (one sixth molar) solution intravenously for alkalization of the urine. From one-half to one liter of sodium lactate solution will suffice to produce urinary alkalinity; if a larger quantity is used, the damaged kidneys may be unable to excrete the excess base and alkalosis may result. As soon as the patient is in acceptable condition for operation, all devitalized tissue is promptly excised, fascial layers are split if the underlying muscle is swollen and tense, or the extremity is amputated if necessary. Gas bacillus and tetanus antitoxins are given prophylactically and chemotherapy is begun. Promptness in institution of treatment is necessary to prevent irreversible renal damage.

### Diagnosis

The diagnosis of shock is all too obvious, but failure to recognize the early or incipient stages is by no means uncommon. Because reflex vasoconstriction will compensate for a considerable loss of blood or plasma, there may be no early indication of shock except the fact that a condition such as the patient has is likely to produce it. If shock is due to loss chiefly of plasma,

as in burns, hemoconcentration will develop within a short time and may be detected by a rise in the hematocrit value. If shock is due to loss of whole blood, as in severe wounds, little change may be found in the blood during the early hours. Later, when shock either has developed or has been averted by treatment, hemodilution may appear as a result of transudation of tissue fluid into the vascular system to replace the lost blood. This sign does not always appear soon enough to be of help in an emergency.

Moon,<sup>2</sup> however, states that hematocrit determinations are of great value in differentiating between shock and hemorrhage and will often serve to detect incipient shock that is not yet clinically evident. He places great emphasis upon the diagnostic value of hemoconcentration.

The pulse rate has not been found to be a reliable index of the loss of blood or plasma; it may remain within normal limits until the appearance of fully established shock. Evans and co-workers<sup>3</sup> and Emerson and Ebert<sup>7</sup> found, however, that there is a definite correlation between the degree of oligemia and systolic blood pressure. The latter authors estimated that, as a rule, systolic pressures below 85 mm. indicate a loss of at least 25 per cent of the blood volume, while systolic pressures above 100 mm. indicate that the blood loss is of less severe degree.

The clinical picture of shock is well known; the patient is seen to be in, or approaching, a state of general collapse and usually is apathetic and indifferent, although conscious. The skin is pallid, cold, and damp, with a clammy feel, and is dewed with a slight perspiration. Occasionally a patient in shock may be nervous, excited, restless, and irritable; in other cases, nausea, vomiting, or perhaps even diarrhea may appear. In the early stages, the pulse rate may be normal, although the pulse pressure and blood pressure decrease progressively. When shock is fully developed, the pulse is rapid, running, thready, and soft, of poor volume, and, in more advanced stages, well-nigh imperceptible. Respirations are rather rapid but are shallow; the temperature is reduced. Perception of pain usually is dulled.

The blood pressure always drops; sometimes it sinks to a point at which even the systolic pressure cannot be read. There is, however, no definite level at which shock can be diagnosed with certainty. A hypertensive or an arteriosclerotic subject may be in shock with a systolic blood pressure considerably higher

than the usually accepted shock level of 80 millimeters. If the blood pressure of the hypertensive patient drops too low to force an adequate blood supply through the generally narrowed arterioles, evidences of tissue anoxia and signs of shock will appear, although the systolic blood pressure may still be at or above 100 millimeters.

### Treatment

**Prophylaxis.**—The best treatment for any surgical complication is prevention. Factors that might lead to the development of shock during or after operation must be recognized and corrected or minimized. Patients with cardiovascular disease, who have little compensatory ability, are very likely to develop this complication. Those with metabolic disorders, such as diabetes mellitus, thyroid disease, or obesity, are treated specifically until the medical complication is controlled as well as possible before operation is undertaken.

The dehydration and malnutrition of old age, alcoholism, starvation, and cachectic disease must be corrected as far as possible. After the fluid and electrolyte balance in these patients has been brought nearer normal, the hemoglobin and red blood cell count should be checked again to detect a possible latent anemia. The increased concentration of the blood often present in dehydrated patients may be responsible sometimes for a deceptively high hemoglobin reading which will drop to a lower level after restoration of the normal blood volume. No major operation may be undertaken safely on a patient whose hemoglobin is below 80 per cent (11.7 Gm.) or whose red blood cell count is below 4,500,000. Transfusions of whole blood are given until this minimum is reached or exceeded. Vitamin deficiencies are noted and corrected.

In the operating room, an infusion of 5 per cent dextrose in distilled water is started, the needle being placed in a vein that is well away from the area of operation. This precaution is always taken before a major operation is begun, so that a blood transfusion can be administered swiftly and without loss of time if the need arises during operation. Veins are collapsed and almost impossible to find after shock has developed, and precious time may be lost in unavailing search. It should be unnecessary to remark that the patient is more likely to have a smooth re-



covery and convalescence if the operator is gentle in his handling of tissues, particularly within the abdomen. Excessive pain, chilling, unnecessary manipulations, and starvation are all preventable factors which might contribute to the development of postoperative shock if overlooked or allowed to occur.

When peripheral circulatory collapse is present or threatened before operation, as in accident or emergency cases, no surgical procedures can be attempted until the danger is over. This is a general rule which may be broken only in cases of massive hemorrhage or respiratory obstruction that are immediate threats to life. All other conditions are only relative emergencies and will permit delay of an hour or two for correction of actual or threatened shock. Any patient who has suffered a sudden injury must be examined for early signs of impending shock before specific surgical treatment is begun. A person may be on the verge of shock and still be able to sit up and talk coherently, although certain premonitory signs usually can be detected. Under such circumstances, the patient is restless and nervous, and the skin is pale, cool, and sometimes clammy. The pulse rate may or may not be elevated, but the blood pressure usually is lower than would be expected in a person who has just been through an exciting or traumatizing experience. Observation of the blood pressure for a few minutes will perhaps show a downward trend. In the presence of vascular depression, so near to actual peripheral circulatory collapse, operative treatment of even a relatively minor lesion may precipitate shock. If the injury is mild, with little loss of blood, shock that develops is likely to be neurogenic or primary in type; if the injury is severe, the more dangerous secondary shock is the type of shock to be feared.

**Therapy.**—Rational treatment of shock must be based on consideration of the causative factors. In cases of *primary shock* in which the neurogenic factor is the chief etiologic agent, for example, collapse during or after spinal anesthesia, vasoconstrictor drugs and cardiovascular stimulants are indicated and probably are more important than intravenous fluids. Ephedrine hydrochloride, 45 mg. (gr.  $\frac{3}{4}$ ), or Methedrine<sup>15</sup> hydrochloride, 20 mg., may be given intramuscularly or intravenously and repeated after an hour or two if necessary. Ephedrine produces a sustained rise of blood pressure and should be used with caution in patients suffering from arteriosclerosis or hypertension. John-

son<sup>16</sup> has advocated the use of Neosynephrine hydrochloride in doses of 0.1 Gm. hypodermically (10 per cent solution), finding no ill effects and obtaining a well-sustained rise in blood pressure. The dose may be repeated at intervals of one hour. Epinephrine is not to be used except as a last resort in a moribund patient and is scarcely indicated even under those circumstances. The stimulant effect of epinephrine on a weakened cardiovascular system is too severe to be safe and too transient to be of value. This drug also produces a postpressor drop in blood pressure which may be fatal to a shocked patient. If the administration of vasoconstrictor and stimulant drugs does not cause an immediate and satisfactory sustained rise in blood pressure, normal salt solution and blood or plasma must be given intravenously at once, for primary shock in surgical patients may progress into much more serious secondary shock as a result of prolonged tissue anoxia.

*Secondary shock* is an emergency of the highest order and corrective measures will be useless if not taken immediately. Treatment is directed toward restoration of the normal blood volume and normal blood pressure, with avoidance of any measure that might add to the severity of the collapse.

Above all, the patient must not be disturbed or moved unless absolutely necessary. Measures are taken to reduce painful stimuli; for example, in severely traumatized patients, fractures may be splinted to prevent further pain or soft tissue damage, but reduction is not attempted until all danger of shock is past. The foot of the bed or stretcher is elevated at least ten inches to improve the cerebral blood supply, and the patient is covered with one or two blankets to conserve body heat. The formerly accepted practice of surrounding the patient with hot-water bottles has been given up, since it is felt that enforced dilatation of the peripheral vessels might withdraw blood from the more vital circulatory channels supplying the viscera and nervous system. Morphine should be used in relatively large doses (16 to 32 mg., or gr.  $\frac{1}{4}$  to  $\frac{1}{2}$ ) to reduce pain and to quiet the patient, but only when definitely indicated for these purposes. It is worth noting that morphine administered subcutaneously may be absorbed slowly, if at all, by the depressed circulation during shock, and that if repeated doses are given because of apparent ineffectiveness, the total amount of the drug may be absorbed

all at once when normal blood pressure is restored, with consequent signs of morphine overdosage. A small dose of morphine given slowly intravenously will be most effective. In any case, care must be taken not to mask the clinical picture in undiagnosed disease or to give opiates in doses large enough to add to the already existing respiratory depression.

Stimulant drugs, which are so useful in primary or neurogenic shock, are of little value in true shock. In this state, the defect lies in the decreased blood volume, and vasoconstriction already is present. Further vasoconstriction as a result of drugs may elevate the blood pressure for a few minutes, but the subsequent drop in pressure may not respond to later transfusion therapy as well as if no drugs had been used. It is almost a natural impulse to use stimulant drugs in shock, however, and it is only to be hoped that the least harmful drugs will be used. Caffeine, Coramine, and perhaps Neosynephrine probably are permissible, but epinephrine should never be used in secondary shock, and ephedrine too is likely to be dangerous. In general, mild vasoconstrictor drugs, therapeutically insufficient in themselves, may help for the few minutes required to prepare an infusion or a blood transfusion.

**BLOOD TRANSFUSION.**—The mainstay of shock treatment is the administration of blood transfusions. Plasma may be substituted for blood to a great extent but cannot replace it. Other substitutes, while even less satisfactory than plasma, are of great help and sometimes may prove sufficient in cases of mild or incipient shock.

The quantity of blood required to restore the circulating blood volume to normal depends on the individual patient, his size, age, and general state of health, on the traumatic influence causing the shock, on the amount the blood volume is decreased, and on the duration of shock before treatment is instituted. Enough blood should be given as quickly as possible to restore the systolic blood pressure to a level of at least 100 mm. of mercury. In some cases this may require transfusion of 1,000 to 2,500 c.c. of blood, with or without additional plasma. Severely traumatized patients who are being prepared for operation do best if given only enough blood to bring them into condition satisfactory for operation. Additional blood then can be given during and after operation as indicated. Full restoration of lost blood

before surgery is begun may cause the wound to bleed afresh, with further local damage and perhaps recurrence of shock. Until about the beginning of World War II transfusions were given in relatively small amounts, although some investigators<sup>17</sup> had pointed out earlier that transfusions, like any other therapeutic measure, should be adjusted to the patient's needs, no matter how small or how large the amount required. Following establishment of the fact that trauma may cause a reduction of up to 40 per cent in blood volume, large transfusions in the treatment of shock have become standard. As a rule, transfusions are given rapidly in case of shock and slowly when the need for blood is less acute.

**PLASMA.**—Plasma is the best possible substitute for blood in treatment of shock, particularly shock due to severe injuries. Blood is not often available at the spot where accidents occur, and, in any case, time is required for proper cross matching before blood transfusions can be given. Shock may develop unexpectedly even in a hospitalized patient, in whom the need for blood transfusion has not been foreseen. Under these circumstances, the administration of plasma, while not therapeutically sufficient in itself, will improve the patient's condition until blood can be obtained for transfusion.

Experience gained during military service has proved that plasma is in no way a complete substitute for blood. The life-saving properties of plasma in the treatment of shock were overrated at the beginning of World War II, and it was soon found that plasma therapy has its limitations. Alone, it cannot be used satisfactorily either to bring a patient out of shock or to prepare a shocked patient for operation; blood is necessary for both these purposes. The value of plasma in the management of shock due to hemorrhage or trauma lies in the fact that it will partially correct the deficit in blood volume and cause elevation of blood pressure to a point above the shock level, and therefore gain time to prepare transfusions of blood. Even though the systolic pressure has been raised to normal, the patient is not an acceptable surgical risk unless the red blood cell count has been improved also. Shock is likely to develop again during or after operation and may not respond a second time to plasma transfusions. A second point of interest is that elevation of blood pressure in injured patients may cause divided vessels in the

wound to bleed again, with further loss of the already depleted red blood cells. To avoid this possibility, transfusions are given until the systolic pressure reaches 90 mm., when operation can be safely begun and blood transfusion started at the same time.

Various formulas and rules have been devised to determine the amount of plasma required in individual cases. For example, Harkins<sup>18</sup> has suggested that 100 c.c. of plasma may be given for each point the hematocrit is raised above a normal of

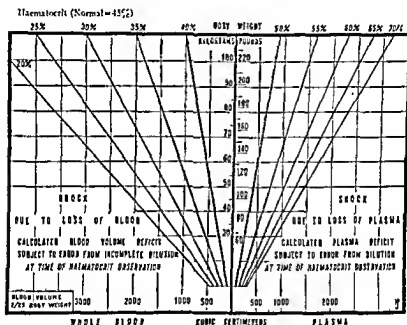


Fig. 10—Requirements for adequate replacement therapy. Follow the diagonal line of hematocrit reading to point of intersection with horizontal line indicating patient's weight and then follow the vertical line down to bottom of chart to determine the required amount of blood or plasma. (From Jenkins, Shafer, and Owens, Jr. Arch Surg 47: 1, 1943.)

45 per cent. Jenkins and associates<sup>19</sup> have devised a nomogram (Fig. 10) to determine the minimum amount of blood or plasma necessary to replace the amount lost. These investigators state that the best index of the relative cellular content of the blood is the hematocrit value, which provides a rough estimate of the degree of hemodilution following blood loss or

the degree of hemoconcentration following plasma loss. This value therefore affords some information concerning the approximate deficit in total blood volume. For establishment of a base line in the nomogram, the normal blood volume was considered as 8 per cent of the body weight and the normal volume of packed red cells (hematocrit) was considered as 45 per cent. Hematocrit values below 45 (hemodilution) usually follow blood loss, with replacement by tissue fluid transudation; proper therapy requires transfusion of whole blood according to the degree of hemodilution. Hematocrit values above 45 (hemoconcentration) usually follow plasma loss with consequent relative decrease in the fluid component of the blood; proper therapy requires transfusion of plasma. However, the blood changes reflected in the hematocrit do not keep pace with the pathologic state; several hours are required for the full effects to develop. Moreover, loss both of plasma and of red cells, such as occurs in severe burns, is not reflected accurately in the hematocrit, the greater loss overshadowing the lesser one. For these reasons, any quantitative rule for blood or plasma replacement based upon the hematocrit value, as in the case of this nomogram, must be considered only as a minimum approximation for the initial dose; repeated hematocrit determinations must be made at frequent intervals.

Under emergency conditions, however, prompt laboratory determinations may not be available, and in many cases in which whole blood is lost, hemoconcentration may not be present. Clinical evaluation of the patient's condition, therefore, is probably the safest guide to therapy. A minimum of 500 c.c. of plasma is given and the blood pressure determined. If the systolic pressure has reached a level of 90 mm., administration may be stopped or continued very slowly until blood transfusions can be secured. The patient normally shows a general improvement as his blood pressure rises, but close watch must be kept upon the blood pressure even after blood loss has been replaced.

While *serum* may be used for transfusion with safety, it has been abandoned almost entirely for this purpose in favor of plasma. Transfusion of serum is often followed by reactions, and the preparation of serum is relatively complicated. The factor of economy enters also, since whole blood yields 10 to 15

per cent less serum than plasma, and in serum the fibrinogen and prothrombin of the blood have been removed

The immediate collection of plasma for emergency use is not possible, plasma is always used as a stored or preserved preparation. The blood is collected from donors under strict surgical asepsis, citrated, and refrigerated, and the plasma is later separated by centrifugation. Plasma also may be collected simply by aspiration of the supernatant clear liquid from bank blood, using either fresh blood or blood that is a little too old to be satisfactory for transfusion as such. Asepsis can be maintained if a sterile vacuum flask is used for aspiration (p. 820). The plasma obtained from a number of donors is pooled, filtered, and distributed into small containers. Cloudy deposits of fibrin may form in stored liquid plasma and filtration is necessary at the time of administration. In this way, each hospital can maintain its own plasma bank in addition to a blood bank.

Stored liquid plasma is kept best in a refrigerator at 4° C., although it is relatively stable even at room temperature. Deterioration occurs in certain components (complement, prothrombin, antibodies) after several days.

A relatively simple process for the preservation of plasma by desiccation has been developed by Flossdorf and co-workers.<sup>20</sup> The desiccated plasma, preserved in bottles as a sterile powder, can be stored indefinitely without necessity for refrigeration and can be reconstituted by redissolving the powder in a quantity of distilled water or of 0.1 per cent citric acid solution equal to the original amount of plasma before processing. During desiccation of plasma, the contained carbon dioxide is lost, so that when the powder is redissolved in distilled water, an abnormally alkaline solution is formed. The use of 0.1 per cent citric acid rather than distilled water therefore has been suggested as a vehicle. Storage in this manner permits the use of concentrated, normal, or dilute plasma in any strength or quantity desired. The Standard Army and Navy Package of Normal Human Plasma, Dried, consists of two 400 c.c. bottles and intravenous equipment in sealed metal cases packed in a waterproof pasteboard box. The dried plasma obtained from 300 c.c. of normal citrated plasma is stored in one of the bottles under a relative vacuum, and the other bottle contains 300 c.c. of sterile distilled water. Equipment is provided for simple reconstitution and admin-

istration of the plasma. This package, used by the thousands during World War II, is now being replaced by a larger unit, carrying dried plasma equivalent to 600 c.c. of normal plasma, on the basis that practically every patient requiring any plasma needs at least two 300 c.c. transfusions.

Plasma, either fresh or preserved, can be given intravenously without cross matching. The isoagglutinins of the plasma are suppressed to a great extent by the pooling of different types, so that agglutination reactions do not occur in transfusions. Plasma usually is given in normal concentration at the same rate of speed as blood transfusions but may be given safely in concentrated form and at a rapid rate when necessary.

Reactions following plasma transfusions are those characteristic of any intravenous therapy. Pyrogenic reactions (p. 184), urticarial reactions on an allergic basis (p. 185), and overloading reactions in cardiac patients may occur.

**CONCENTRATED HUMAN SERUM ALBUMIN.** — Concentrated human serum albumin was developed<sup>21\*</sup> as a substitution for plasma used in the military service when space was at too much of a premium to permit transportation of the standard plasma package. Albumin, which composes 60 per cent of the plasma protein content, accounts for more than 80 per cent of the colloid osmotic pressure of the plasma. It is stable, of low viscosity, and highly soluble in water, so that it may be made up into a concentrated aqueous solution and stored without refrigeration until time for use. Cross matching is not necessary. Experimental work has demonstrated that the high colloid osmotic pressure exerted by serum albumin enables each gram to hold 18 c.c. of fluid in the vascular system, so that 25 Gm. of serum albumin is osmotically equivalent to 450 c.c. of plasma (500 c.c. of citrated plasma). The Standard Army and Navy Package of Serum Albumin therefore consists of a flask containing 25 Gm. of human serum albumin in 0.3 molar sodium chloride at pH 6.8, together with equipment for intravenous administration.

After administration of concentrated serum albumin, there is a drop in the hematocrit reading and cell counts as a result of transudation of tissue fluid into the blood stream. The

\*In the laboratories of E. J. Cohn, Harvard University.



plasma protein values are not depressed, however, because the passage of fluid into the vascular system is a response to the introduction of albumin. Concentrated albumin cannot be used satisfactorily in the presence of dehydration, in which there is depletion of the tissue fluids. Under such circumstances, the therapeutic effectiveness of albumin is enhanced by the simultaneous administration of normal salt solution by any route available. No reactions have been noted following the administration of human serum albumin, which is not antigenic and carries no isoagglutinins. If concentrated serum albumin is used in treatment of shock, transfusions of blood must be given as soon as possible, even though improvement occurs following administration of albumin, since the lost red blood cells also must be replaced.

**SUBSTITUTE COLLOIDS.**—Because human blood and its derivatives are not always available in the necessary amounts, various substitutes have been studied. The primary need, of course, is for an inexpensive nontoxic material procurable in large quantities that can be easily prepared and administered as a solution isotonic with blood and that will not only produce a colloid osmotic pressure equivalent to that of blood, but will remain in the circulatory system long enough to assure restoration of blood volume and recovery from shock.

*Gum acacia*, as a 6 per cent solution in normal salt solution, was introduced at the time of World War I and was used with more or less satisfactory results for a number of years. The large molecules of the gum do not pass across the capillary membrane and the intravascular osmotic tension therefore is effectively increased. *Gum acacia* is not broken down in the body but is picked up and stored indefinitely by the reticulo-endothelial cells, particularly in the liver. Depression of liver function follows, with an irreducible proportion of deaths that, although small, renders use of *acacia* inadvisable except in an acute emergency when no more suitable substance is available.

*Gelatin* seems at present to be the most promising substitute for plasma in the emergency treatment of shock and preshock states. Gelatin made from the bones of cattle (osseine gelatin,<sup>23</sup> Knox P-20) and prepared according to special methods is administered intravenously in 4 to 6 per cent concentration in

normal salt solution in any quantities required. Edible gelatin is not satisfactory for intravenous use. Care in preparation is necessary and the use of commercially manufactured and sterilized solutions is safest.

Gelatin is stable and may be heat-sterilized and stored without refrigeration. Since gelatin solution at room temperature is in the gel phase, it is necessary to liquefy the solution before administration by immersing the flask in a basin of water at from 100 to 110° F.; care must be taken to avoid overheating. The solution is somewhat viscous; an 18 or 19 gauge needle is required for average rates of administration. Some difficulty may be encountered in typing blood following administration of gelatin<sup>23</sup> intravenously; blood samples for typing and cross matching should be drawn before gelatin is given.

Koop<sup>24</sup> states that ossein gelatin solutions are definitely superior to all plasma substitutes studied so far except those derived from human blood. This writer finds that administration of ossein gelatin produces no reactions and no toxic effects and that it is as effective as plasma in the treatment of shock due to hemorrhage and burns. The increase in blood volume following administration of ossein gelatin is said to be maintained for as long as twenty-four hours. Properly prepared gelatin is not in wide use at the present time; it apparently offers much promise as an effective plasma substitute, but clinical use has been restricted to a relatively small number of medical centers.

*Pectin*, a hemicellulose occurring in certain fruits and responsible for their jellying properties, has been advocated by Hartman and co-workers<sup>25</sup> for use as a plasma substitute. A solution of 0.5 per cent pectin in normal salt solution produces a colloidal osmotic pressure approximately equivalent to that of plasma and, when given intravenously, pectin solution is fairly effective in temporarily restoring the blood volume in shock. Pectin, however, is taken up by the liver and may cause depression of liver function; other visceral damage<sup>26</sup> also may be produced. The disadvantages of pectin solution make its general use inadvisable.

*Bovine serum albumin* is being investigated experimentally with regard to use as a plasma substitute<sup>27</sup> in treatment of shock. Although pure crystalline preparations free of all but minute

traces of globulin have been prepared, the high incidence of moderately severe and incapacitating delayed reactions following its use render it still unsafe for clinical administration. Methods of despeciation, which may eliminate its antigenicity, are being currently investigated.

**NORMAL SALT SOLUTION.**—Normal salt solution, formerly the mainstay of treatment for shock during the period of time required for preparation of blood transfusions, has been replaced for this purpose by plasma. It is claimed by some authors that the value of normal salt solution in treatment of shock is generally underestimated, however. Allen<sup>28</sup> has continued to advocate the use of normal salt solution rather than plasma as the preferred treatment for shock to correct the sodium deficiency which develops as a result of the transfer of electrolytes from the blood into the tissues. He states that administration of normal salt solution will correct the hemoconcentration of shock by transforming it into a state corresponding to hypoproteinemia with adequate but diluted blood volume. Fox<sup>29</sup> has reported good results in the prompt early treatment of burn shock with large quantities of isotonic solutions of sodium salts (sodium lactate), preferably by mouth. It is generally believed, however, that normal salt solution may be of some use in prevention or supportive treatment of shock but that it is inadequate as therapy. Davis<sup>30</sup> has shown that the stimulant effect of intravenous fluids in treatment of shock lasts only as long as the fluid remains in the blood stream and seems to depend on the resultant increase in blood volume and blood flow. Although the blood volume is increased temporarily by this means, the crystalloid solution leaves the vascular system rapidly, carrying some protein with it, particularly into the traumatized area. This washing-out of plasma protein results in a further decrease in plasma osmotic pressure. For these reasons, it is felt that the amount of normal salt solution that may be given safely to a shocked patient is limited and should be supplemented as soon as possible by blood or plasma transfusion. Normal salt solution therefore is given in quantities of 1,000 to 1,500 c.c. while the transfusion is being prepared, and in these amounts may be of value.

The use of *adrenal cortical extract* or of the synthetic desoxycorticosterone acetate has been suggested to correct the

altered permeability of the capillaries in shock, particularly in shock due to burns. No well-defined beneficial effects have been observed, and there have been indications that overdosage of adrenal cortical hormones may be actually harmful. Employment of adrenal substances in the treatment of shock is not advised.

The use of pure (100 per cent) oxygen has been advocated to increase the oxygen saturation of the blood and tissues. Boothby, Mayo, and Lovelace<sup>11</sup> advise that since anoxemia is a major factor in the development and continuation of shock, 100 per cent oxygen should be administered as an adjunct both in prevention and treatment of surgical and traumatic shock. Work done during World War II on patients in shock has failed generally to show that administration of oxygen is of definite value. Its use has not yet been abandoned, since it will do no harm and may be helpful in some cases.

### Summary

1. Primary shock or syncope is a reflex vasodilatation in response to nervous overstimulation and is marked by faintness, pallor, and reduced blood pressure. It is unaccompanied by loss of blood or plasma from the vascular system and, like the fall in blood pressure accompanying spinal anesthesia, is best treated by stimulant drugs. Caffeine sodiobenzoate, 0.5 Gm. (gr.  $7\frac{1}{2}$ ), may be given hypodermically or intravenously, or ephedrine hydrochloride, 45 mg. (gr.  $\frac{3}{4}$ ), Methedrine hydrochloride, 20 mg., Neosynephrine hydrochloride, 0.1 Gm., or Metrazol, 0.1 to 0.2 Gm., may be given hypodermically or intramuscularly.

2. Secondary shock may be due to any one or any combination of a number of causes, chief among which are trauma and hemorrhage. This is the dangerous type of shock and must be recognized early in its course for treatment to be effective. It is due chiefly to loss of plasma or blood or both from the vascular system and can be recognized best in its incipient stages by a drop in systolic blood pressure to 85 mm. or less following an injury or blood loss capable of producing shock. Hemoconcentration is another indicative sign.

3. Prevention of shock is far more effective than treatment. Before a serious surgical operation is undertaken, factors which

might contribute to shock must be corrected, blood volume and blood hemoglobin restored to a safe level, and whole blood made available for immediate use through an intravenous set already in operation before the incision is made. Blood transfusions are given until the systolic blood pressure is maintained at 85 to 100 mm. before emergency operation is undertaken.

4. Treatment of secondary shock includes maintenance of body heat with blankets rather than with hot-water bottles, avoidance of any unnecessary movement or further trauma, elevation of the foot of the bed to improve venous return, administration of one or, at most, two doses of morphine if indicated, avoidance of use of stimulant drugs, and immediate administration of whole blood or blood substitutes by transfusion. For treatment of crushing injuries, the use of sodium lactate (one-sixth molar) solution intravenously has been suggested in doses of 500 c.c., repeated as necessary to alkalize the urine.

Of the blood substitutes, the following, in descending order of value, are the most efficacious: plasma, concentrated human serum albumin together with normal salt solution, and specially prepared ossein gelatin in 4 to 5 per cent concentration in normal salt solution. Pectin in 0.5 per cent solution and gum acacia in 6 per cent solution are effective but may cause visceral damage. Normal salt solution is believed by some to be the most efficacious fluid available for treatment of shock, even superior to plasma, but is generally considered to be of use only as a temporary measure until whole blood or a blood substitute can be obtained. Whatever its true value in this respect, normal salt solution should certainly be given intravenously to elevate and sustain the blood pressure until other suitable fluids, particularly whole blood and plasma, are available.

Pure oxygen has been advised, but its value has never been established. Adrenal cortical extracts also are of very questionable value.

### References

1. Blalock, A.: Consideration of Present Status of Shock Problem; "Problems on Shock," *Surgery* 11: 487, 1943.
2. Cannon, W. B.: Medical Department U. S. Army in the World War, Washington. Surgeon-General's Office: 1923; 11, 186.
3. Moon, V. H.: Dynamics of Shock and Its Clinical Implications, *Internat. Abstr. Surg.* 79: 1, 1944; in *Surg., Gynec. & Obst.*, July, 1944.

4. Parsons, E., and Phemister, D. B.: Hemorrhage and "Shock" in Traumatized Limbs; Experimental Study, *Surg., Gynec. & Obst.* 51: 196, 1930.
5. Blalock, A.: Acute Circulatory Failure as Exemplified by Shock and Hemorrhage (Arthur Dean Bevan Lecture), *Surg., Gynec. & Obst.* 58: 551, 1934.
6. McDowall, R. J. S.: Circulation in Relation to Shock, *Brit. M. J.* 1: 919, 1940.
7. Emerson, C. P., and Ebert, R. V.: A Study of Shock in Battle Casualties. Measurements of the Blood Volume Changes Occurring in Response to Therapy, *Ann. Surg.* 122: 745, 1945.
8. Evans, E. I., Hoover, M. J., James, G. W., and Alm, T.: Studies on Traumatic Shock: I. Blood Volume Changes in Traumatic Shock, *Ann. Surg.* 119: 64, 1944.
9. Bywaters, E. G. L., Delory, G. E., Rimington, C., and Smiles, J.: Myohaemoglobin in Urine of Air Raid Casualties With Crushing Injury, *Biochem. J.* 33: 1164, 1941.
10. Dunn, J. S., Gillespie, M., and Niven, J. S. F.: Renal Lesions in Two Cases of Crush Syndrome, *Lancet* 2: 549, 1941.
11. Patey, H. D., and Robertson, J. A.: Compression Treatment of Crush Injuries of Limbs, *Lancet* 1: 780, 1941.
12. Corcoran, A. C., and Page, I. H.: Crush Syndrome: Post-Traumatic Anuria, *J. A. M. A.* 134: 436, 1947.
13. Franklin, K. J., Barclay, A. E., Daniel, P., Trueta, J., and Pritchard, M. M. L.: Renal Pathology in the Light of Recent Neurovascular Studies, *Lancet* 2: 239, 1946.
14. Lucké, B.: Lower Nephron Nephrosis: The Renal Lesions of the Crush Syndrome, of Burns, Transfusions and Other Conditions Affecting the Lower Segment of the Nephron, *Mil. Surgeon* 99: 371, 1946.
15. Dripps, R. D., and Deming, V. N.: An Evaluation of Certain Drugs Used to Maintain Blood Pressure During Spinal Anesthesia. Comparison of Ephedrine, Paredrine, Pitressin-Ephedrine, and Methedrine in 2,500 Cases, *Surg., Gynec. & Obst.* 83: 312, 1946.
16. Johnson, C. A.: Neo-Synephrin Hydrochloride in Treatment of Hypotension and Shock From Trauma or Hemorrhage, *Surg., Gynec. & Obst.* 65: 458, 1937.
17. Lundy, J. S., Tuohy, E. B., and Adams, R. C.: Annual Report for 1937 of the Section on Anesthesia; Including Data on Blood Transfusion, *Proc. Staff. Meet., Mayo Clin.* 13: 177, 1938.
18. Harkins, H. N.: Problem of Thermal Burns, *J. A. M. A.* 125: 533, 1944.
19. Jenkins, H. P., Schafer, P. W., and Owens, F. M., Jr.: Guide to Replacement Therapy for Loss of Blood or Plasma, *Arch. Surg.* 47: 1, 1943.
20. Florsdorf, E. W., Stokes, F. J., and Mudd, S.: Desivac Process for Drying From Frozen State, *J. A. M. A.* 115: 1095, 1940.

21. Janeway, C. A.: Clinical Use of Products of Human Plasma Fractionation I Albumin in Shock and Hypoproteinemia II Gamma-Globulin in Measles, *J. A. M. A.* 126: 674, 1944.
22. Janeway, C. A., Gibson, S. T., Woodruff, L. M., Heyl, J. T., Bailey, O. T., and Newhouser, L. T.: Concentrated Human Serum Albumin; Albumin in Treatment of Shock; Safety of Albumin, Albumin in Treatment of Hypoproteinemia, *J. Clin. Investigation* 23: 465, 1944.
23. Evaluation of Studies on Gelatin Preparations for Intravenous Use. Special Report from the National Research Council, *J. A. M. A.* 125: 285, 1944.
24. Koop, C. E.: The Use of Specially Prepared Gelatin Solution as a Plasma Substitute, *S. Clin. North America* 24: 1300, 1944.
25. Hartman, F. W., Shelling, V., Harkins, H. N., and Brush, B.: Pectin Solution as Blood Substitute, *Ann. Surg.* 114: 212, 1941.
26. Popper, H., Volk, B. W., Meyer, K. A., Kozoll, D. D., and Steigmann, F. W.: Evaluation of Gelatin and Pectin Solutions as Substitutes for Plasma in Treatment of Shock; Histologic Changes Produced in Human Beings, *J. Lab. & Clin. Med.* 30: 352, 1945.
27. State, D., Romero, F. R., Castellanos, M. M., and Wangenstein, O. H.: Clinical Evaluation of Bovine Serum Albumin as a Blood Substitute, *Surgery* 22: 424, 1917.
28. Allen, F. M.: Theory and Therapy of Shock; Varied Fluid Injections, *Am. J. Surg.* 62: 80, 1943.
29. Fox, C. L., Jr.: Oral Sodium Lactate in Treatment of Burn Shock, *J. A. M. A.* 121: 207, 1944.
30. Davis, H. A.: Physiologic Availability of Fluids in Secondary Shock, *Arch. Surg.* 35: 461, 1937.
31. Boothby, W. M., Mayo, C. W., and Lovelace, W. R., Jr.: One Hundred Per Cent Oxygen; Indications for its Use and Methods of its Administration, *J. A. M. A.* 113: 477, 1939.

## CHAPTER 8

# TRANSFUSION

### Indications

Before World War II it was generally believed that plasma would serve as a highly satisfactory emergency substitute for blood in practically every instance in which transfusion of blood might be required. Experience has shown, however, that when there has been a loss of red blood cells, whether external or concealed, nothing can substitute fully for blood transfusion. In general, transfusion of blood substitutes will raise blood pressure, restore depleted blood volume, elevate subnormal plasma proteins, and gain time in an emergency for the preparation of a blood transfusion. Transfusion of blood itself will serve all these purposes and will replace lost hemoglobin as well. Moreover, transfusion is no longer employed only in the desperately ill patient but has a place in the regular treatment of many less urgent conditions. Among the indications for blood transfusion are the following:

**Hemorrhage.**—It is difficult to estimate roughly the amount of blood lost following a traumatic accident, a hemorrhage from the gastrointestinal tract, or a surgical operation. The surgeon rarely realizes that the sum of the small amounts of blood on each sponge and pack and in each clot reaches a highly significant total. A dangerous loss of blood may be quite unsuspected unless the operator is aware beforehand of the average amounts lost in each type of operation. This is especially true in the infant, whose total blood volume may not exceed 400 cubic centimeters. Every drop of blood counts in small children, and during an operation each vessel divided must be instantly clamped and ligated. An additional few minutes spent at various stages of any operation, whether it is in a child or an adult, to clamp and ligate bleeding vessels or to suture oozing areas or to pack bleeding surfaces may save the patient from developing shock during or after operation. It is worth while to remember also that no matter how careful the hemostasis, there is always an irreducible minimum of blood lost at any opera-



tion, and when the surgical procedure is a major one, the blood loss is always relatively large.

Crook, Ioh, and Collier<sup>1</sup> have made careful studies of blood loss during representative major surgical procedures; their findings are summarized in Table III.

TABLE III. EXTENT OF BLOOD LOSS DURING MAJOR SURGICAL OPERATIONS  
(Modified from Crook, Ioh, and Collier: Surg., Gynec. & Obst., 82:417, 1946.)

OPERATION	RANGE OF BLOOD LOSS (c.c.)	AVERAGE BLOOD LOSS (c.c.)	AVERAGE DECREASE IN TOTAL BLOOD VOLUME (%)	OPERATING TIME (MIN.)
Biliary tract operations	158-1,455	594	14.6	105-255
Radical breast amputations	529-1,091	803	17.4	143-249
Stomach operations	321- 804	599	6.8 to 20.0	155-287
Resection of rectum	183- 686	410	9.5	107-245
Thyroidectomy	204- 725	373	10.7	58-140

As these workers have pointed out, the blood loss at operation is usually greater than a casual estimate would indicate, and best results are obtained when the blood is replaced as it is lost, during the surgical procedure rather than after. Untoward symptoms or slow recovery following operation often are attributed to the trauma of the surgical procedure or to the patient's poor constitution and general health, when it is more than probable that weakness and delayed convalescence reflect a significant and unsuspected blood loss. Hemorrhage of this type is not always evidenced by changes in the hematocrit reading or blood counts. It is true that blood loss is followed by tissue fluid transudation into the vascular system until osmotic relationships are restored to normal, but it is not necessarily true that the amount of blood lost by hemorrhage will be replaced by transudation with an exactly equal or even approximately equal amount of fluid. If such a reduction in blood volume occurs, the hematocrit

and red cell count will not be depressed in proportion to the hemorrhage. Furthermore, plasma loss in the region of the operation may occur and may lower the total blood volume still further.

For these reasons, the probable loss of blood for each type of operation should be anticipated and considered in relation to the patient's general condition. Transfusion of the proper amount of blood may be given during operation and additional amounts later as indicated for supportive therapy.

No blood substitute is satisfactory; whole blood is the only proper therapy for blood loss. There is no fixed amount that can be advocated in any case. The patient must receive enough to bring the blood pressure, blood volume, and oxygen-carrying capacity up to a level near normal. Although transfusions are usually given slowly, the rate of administration during an emergency is governed only by the patient's need and response. From 2,000 to 3,000 c.c. of blood may be needed when blood loss is extreme, and, in any case, the amount given is determined solely by the patient's requirement, whether it is 250 or 2,500 cubic centimeters.

Replacement of blood lost by acute hemorrhage is an emergency procedure. Hypotension and anoxia of severe degree may produce lasting visceral damage or even irreversible shock in relatively few minutes. While plasma is of value as a temporary measure, it is better to use only enough to raise the blood pressure safely above the shock level without trying to restore normal blood pressure and blood volume in the absence of sufficient red cells to restore normal oxygenation of tissues.

**Shock.**—Collapse due to hemorrhage can be treated safely only by blood transfusion. Shock due chiefly to plasma loss is followed by hemoconcentration and increased blood viscosity, so that transfusion of whole blood may seem less desirable than transfusion of plasma alone. As a matter of fact, shock due to loss of plasma alone is not common outside the laboratory; even in shock due to burns, the usual example cited of shock with hemoconcentration, there is considerable red cell destruction with subsequent anemia. Shock due to trauma is accompanied by significant loss of red blood cells as well as plasma into the injured tissues. It is probably true, therefore, that in shock

due to trauma of any kind or in postoperative shock, transfusion of blood is always more desirable than transfusion of plasma alone. After a satisfactory pressor response has been obtained, further fluid administration may be judged according to hematocrit determinations, red cell counts, total plasma proteins, serum albumin concentration, and plasma specific gravity.

Although a great deal has been written on the mechanism and manifestations of shock, on the methods of determining its cause, type, and severity, and on the methods of deciding what therapeutic agent to use and how much to give, the clinical state of the patient and the clinical response to treatment will be the most dependable guides to therapy for the average surgeon. From this standpoint it will always be safest, as demonstrated in World War II, to administer plasma or other blood substitutes immediately but only until blood can be secured and matched and then to give blood until a satisfactory clinical response is secured.

Massive transfusions of plasma in patients suffering from traumatic shock may be actually harmful, just as they are in hemorrhagic shock (p. 139). Plasma therefore is given only in sufficient quantity to maintain the systolic blood pressure at 85 to 100 mm. of mercury until compatible blood has been secured.

**Preoperative and Postoperative Care.**—In any case, prevention of shock is always simpler and safer than treatment of shock. For this reason, blood transfusion is no longer used only to avert impending death but is one of the most useful methods of improving a patient's general condition. While it is not quite accurate to say that blood transfusion properly and adequately used will convert a poor surgical risk into a good one, it is certainly true that blood transfusions will often improve the condition of a desperately ill patient enough to make him an acceptable surgical risk.

Blood transfusion is of particular value in surgical patients in the correction of secondary anemia, hypoproteinemia, malnutrition, and general debility. These debilitating states occur as either primary or secondary effects in patients suffering from such conditions as gastrointestinal tract diseases inter-

fering with intake and absorption of food, malignant lesions causing depression of general health, malnutrition with resultant disturbances in all the bodily functions, or severe chronic suppurative diseases with constant loss of body protein and absorption of toxic products. Plasma may serve temporarily to replenish lost proteins, but correction of the dehydration almost always present in such cases may reveal anemia, which requires transfusion of blood for correction. A single transfusion of 500 c.c. is usually not enough in such patients; enough blood should be given to correct the abnormal state.

The normal red blood cell count averages 5,000,000 per cubic millimeter in men and 4,500,000 in women. The hemoglobin concentration varies but may be considered arbitrarily as 14.6 Gm per 100 cubic centimeters. In accordance with the normal red cell count, the normal hemoglobin would amount to 14.6 Gm (100 per cent) in men and 13.1 Gm. (90 per cent) in women. Patients with a hemoglobin level below 80 per cent (11.7 Gm.) or a red blood cell count of 4,500,000 or less are not acceptable for major elective surgery until the anemia has been corrected.

**Hemorrhagic States.**—Reduced to the simplest form, the processes involved in blood clotting are as follows:

$$\begin{aligned}\text{Prothrombin} + \text{calcium} + \text{thromboplastin} &= \text{Thrombin} \\ \text{Thrombin} + \text{fibrinogen} &= \text{Fibrin}\end{aligned}$$

Prothrombin, calcium, and fibrinogen are present in the circulating blood. Thromboplastin is supplied by the platelets, which disintegrate upon contact with air or with any surface other than smooth endothelium. Thromboplastin is present also in the tissues, and tissue substance or tissue extracts will serve to induce clotting. Other factors in the blood affect the clotting mechanism; for example, antiprothrombin, which restrains the activity of prothrombin even in the presence of calcium and thromboplastin ordinarily sufficient to induce clotting. It is probable that heparin acts as an antiprothrombin, while sodium citrate prevents clotting by inactivating the blood calcium.

Certain blood disorders caused by lack or insufficiency of one of the factors involved in clotting are characterized by a tendency to spontaneous hemorrhage or to prolonged bleeding.

Most of them, for example, hemophilia and thrombocytopenic purpura, require blood transfusion to supply temporarily enough of the missing factor to permit operation or to control continuing hemorrhage (p. 225). Other hemorrhagic disorders, like hypoprothrombinemia, may be controlled indirectly by promoting formation of the missing factor (p. 706). Extensive liver disease, however, sometimes may prevent a response to therapy with vitamin K, and transfusions of fresh blood will be necessary to supply enough of the deficient prothrombin (and fibrinogen) until the liver function can be improved.

### Contraindications

When transfusion of blood is indicated for corrective therapy, there are very few conditions that might interfere with its use. Cardiac disease or damage is a reason for slow and cautious administration of blood but is not a contraindication to transfusion unless actual cardiac decompensation is present. To prevent cardiac failure from developing as a result of sudden overloading of the circulation, necessary blood transfusions are given by the drip method, adjusted to deliver not more than 30 drops per minute. At this rate, approximately two hours will be required for the administration of 250 c.c. of blood. In such cases it is better to give small transfusions at intervals to permit slow circulatory adjustment to the increased volume.

Signs of pulmonary congestion, appearance of dyspnea or cardiac pain, or any evidence of impending transfusion reaction require immediate discontinuance of the transfusion. Just as a low cardiac reserve necessitates caution in use of transfusions, so does a diminished renal reserve. Although a mild transfusion reaction may produce little effect on normal kidneys, total anuria may result if the kidneys are damaged by chronic disease.

Transfusion of blood of course is contraindicated in the presence of failure of the pulmonary circulation because of cardiac disease, pulmonary edema for other reasons, or pulmonary embolism. Embolism may produce a shocklike clinical picture, and careful diagnosis therefore is necessary.

## Blood Grouping and Cross Matching

Before a blood transfusion can be performed, the type of the subject's blood must be determined and a compatible supply secured. Human blood is subdivided into four serologic groups on the basis of the substances originally described by Landsteiner as isoagglutinins and later investigated more fully by Moss. Briefly, there are considered to be two distinct substances found in human blood serum capable of agglutinating the red blood cells of other individuals (serum agglutinin A and serum agglutinin B). The red cells are thought to contain receptors (A and B) complementary to these substances and the union of a specific serum agglutinin with its specific cell receptor substance is believed to produce agglutination of the cells. The existence of two different serum agglutinins makes possible four different types of blood; both, either, or none of the specific substances may be present in the serum. In each type of case the specific complementary receptor substances in the red cells are necessarily absent.

These substances are constant throughout life with respect to the red blood cells; the specific group is hereditary in character and does not change. Isoagglutinins in the serum are not invariable and may be altered to some extent. The blood group of the individual is therefore determined by the type of the red cells.

When a blood transfusion is given, the donor's plasma is immediately diluted by the large quantity of the recipient's plasma with which it is mixed; any tendency of donor's serum to agglutinate the recipient's cells consequently may be ignored. On the other hand, if the donor's cells are agglutinated by the recipient's serum, multiple emboli and products of hemolysis are formed and a severe, possibly fatal, reaction always ensues.

LANDSTEINER GROUPING	MOSS GROUPING	AGGLUTININS IN SERUM	COMPATIBILITY
AB (Cells)	I	O	Universal recipient
A	II	B	With same group only
B	III	A	With same group only
O	IV	AB	Universal donor

Broadly speaking, any blood sample is compatible with that of another member of the same group. Except for the Rh type (p. 169), subgroups are not of great clinical importance. Type

I serum (Moss) contains no specific isoagglutinins, therefore any type of blood may be used in an emergency for transfusion to recipients of this group. the donor's cells will not be agglutinated. Type IV serum contains both specific substances, but the cells will not be agglutinated by any type of serum. This type of blood may be used safely for transfusion to any type of recipient. It is, of course, always preferable to use donor blood of the same group as that of the recipient whenever possible. Low-titer type IV blood of the Moss grouping (type O, Landsteiner), containing only a low concentration of isoagglutinins in the serum, is preferable to high-titer blood of this "universal donor" group for transfusion to a recipient who is of a different blood type. Witelsky and co-workers<sup>2</sup> have demonstrated that addition of purified A and B group-specific substances will reduce a high titer of serum isoagglutinins to a low level and therefore will reduce the severity and the frequency of the reactions<sup>3</sup> which occasionally follow rapid transfusion of blood of the "universal donor" group into patients of other blood groups.

Probably the best method of securing compatible donors is to determine the blood grouping of the recipient and then determine the blood type of each prospective donor until several of the proper group have been secured. This may easily be done if a supply of types II and III (Moss) serum is kept in the laboratory icebox. The test is performed by placing a drop of Group II serum and a drop of Group III serum at opposite ends of a glass slide and then mixing a small drop of the individual's blood with each. The platinum wire loop used for carrying and mixing the drops must be flamed each time it is used to avoid contaminating one serum specimen with the other. The slide is agitated gently for several minutes and then is inspected under a microscope. The test is read as follows:

GROUP II SERUM	GROUP III SERUM	GROUP OF SPECIMEN
Agglutination	Agglutination	I (Moss)
No change	Agglutination	II (Moss)
Agglutination	No change	III (Moss)
No change	No change	IV (Moss)

Donors of the same blood group as the recipient are selected and cross matching of the two individual blood samples is performed. A strong, healthy donor, preferably male, should be

chosen. It is usually best to avoid taking blood from a donor who has eaten a heavy meal or drunk alcoholic liquors a short time before or who has recently been exercising. If blood from such an individual is used, toxic substances or fatigue products may be transfused into the blood stream of the patient.

Simple determination of blood type is carried out with a drop of blood obtained by pricking the subject's finger tip. Serum samples may be secured by allowing a small amount of blood to clot in a tube. The retracted clot is separated and removed, leaving the clear serum. Red blood cell suspension may be obtained by placing a drop of blood into a tube containing several cubic centimeters of normal salt or sodium citrate solution (2 per cent). Each tube should be labeled with the greatest care to avoid any possibility of mixing specimens from different individuals.

Even though the prospective donor and the recipient are of the same blood group, it is always necessary to make cross preparations, the serum of each individual being matched against the red cells of the other in order to determine complete compatibility of the two bloods. This procedure never may be omitted under any circumstances, even though the same donor may have given blood to the same recipient before. The test usually is carried out by mixing a drop of serum from one individual with a drop of suspension of washed red blood cells from the other. Each preparation is made upon a separate cover slip, which is inverted carefully upon a hollow-ground slide rimmed with petroleum jelly to prevent evaporation, and agitated gently for from five to twenty minutes. If agglutination of the cells does not occur within this time, the bloods are compatible and transfusion may be performed. The more important specimen of the two, for the reasons mentioned previously, is the one matching the donor's cells with the recipient's serum. If any sign of agglutination is noted in this preparation, the bloods should be considered as incompatible. Rouleaux formation is not a sign of incompatibility; hemolysis or formation of irregular clumps does indicate that the two bloods are incompatible.

Rouleaux formation may occur<sup>4</sup> when the cell suspension has been made too concentrated. Rouleaux may be identified by the characteristic formation of columns or "stacks" of red cells, which will usually break up if the preparation is diluted with a drop of normal salt solution or is stirred gently. Agglutination,



on the other hand, will be unaffected by dilution of the test preparation and will be intensified by stirring or agitation.

Rarely, a false incompatibility reaction will be caused by the presence of cold agglutinins<sup>5</sup> in the recipient's serum. Cold agglutinins are not type specific but will cause clumping of donor red cells of any blood group at temperatures between 5 and 20° C. They are present in a high percentage of normal subjects but only rarely are found in sufficient concentration to produce a recognizable effect. Recent reports indicate that cold agglutinins frequently are found in high concentration in the blood of patients suffering from virus pneumonia or from acute hemolytic anemia<sup>6</sup> secondary to sulfonamide toxicity. Cross matching preparatory to giving transfusions to such patients therefore should be done with blood and serum samples at incubator temperatures rather than at room or refrigerator temperatures. The same precaution should be taken with any cross-matching tests when unexpected or inexplicable agglutination<sup>7</sup> occurs.

In such cases, the Landsteiner-Levine test tube method of cross matching blood samples perhaps is preferable to the slide method, because it is more sensitive to weak agglutinins and is better adapted for use at incubator temperature. The technique is simple: 1 drop of recipient's serum, 2 drops of a thin suspension of donor's red cells, and 1 drop of normal salt solution are placed in a Kahn or Hinton tube, mixed, and incubated for thirty minutes. The tube then is centrifuged at a very slow speed for one minute, after which the specimen is examined for agglutination with a magnifying lens. Agglutination, when present, also may be seen grossly if the tube is shaken several times. A final reading is made by low-power microscopic examination of a drop of the mixture on a slide.

Agglutination because of cold hemagglutinins does not render blood unfit for transfusion if it is otherwise compatible. However, the blood should be warmed before being administered, either by allowing the bottle to remain at room temperature for several hours or by placing the container in a basin of water at 95° F. (not over body temperature).

The cross-matching preparation should be checked by two responsible individuals who are familiar with such tests in order to avoid any possibility of error.

No donor should be used who is suffering from a chronic infectious disease that may be transmitted by the blood; for example, malaria or syphilis. Blood used for transfusion must always be subjected to a standard test for syphilis, the Wassermann reaction being the most widely accepted test. If the transfusion is an emergency one, a Kahn, Eagle, or Hinton test for syphilis may be carried out while preparations for the transfusion are under way. The Laughlen serologic test is especially adapted for use in emergencies, for it is simple to perform and to read. This test may be carried out by the intern with no difficulty and it requires only ten minutes for completion.<sup>8</sup> No blood should be transfused into a recipient until the absence of syphilis has been established, both by laboratory test and by examination and questioning of the donor. When the emergency is extremely urgent and the time necessary for serologic tests is lacking, a blood transfusion may be given from a compatible untested donor, preferably a member of the patient's family, but only if the situation is first explained to the relatives and authorization secured.

**Rh Blood Type.**—The explanation for certain previously unclassified transfusion reactions as well as for the pathogenesis of erythroblastosis fetalis became evident following the discovery of the Rh blood group factor. Landsteiner and Wiener in 1940<sup>9</sup> found that agglutinins which developed in the serum of rabbits against the red blood cells of the *Macacus rhesus* monkey would also agglutinate human red blood cells in a high percentage of cases. The reacting substance, or agglutinin, present in human erythrocytes was called the Rh factor because of its original discovery in the erythrocytes of the rhesus monkey.

Human red blood cells therefore can be divided into two main types with reference to this factor. Rh-positive cells contain the specific agglutinin, while Rh-negative cells contain none. The Rh factor has no relation to blood group or to sex but is transmitted genetically<sup>10</sup> as a dominant characteristic. Approximately 85 per cent of all people are Rh positive (92 per cent of Negroes are Rh positive) and the remainder Rh negative.

Introduction of Rh-positive blood into the circulation of the Rh-negative recipient produces no reaction on the first occasion. As a result of the transfusion, anti-Rh agglutinins develop in the serum of the Rh-negative recipient. Transfusion of Rh-positive

blood on a second occasion therefore may result in agglutination and hemolysis of the donor's red cells by the recipient's serum. Transfusion reactions on the basis of Rh incompatibility can occur in no more than 15 per cent of the population, and of these susceptible individuals, sensitization must have occurred as a result of a previous transfusion of Rh-positive blood. The incidence of such reactions consequently is small, particularly since the titer of antibodies may be too low to produce clinical reaction in many cases in which it could be expected.

From seven to ten days are required for sensitization to develop<sup>12</sup> following the first administration of Rh-positive blood to an Rh-negative patient. If a second similar transfusion is given before this much time has elapsed, either no reaction or a very slight reaction will ensue. Transfusion of Rh-positive blood may produce a fully developed transfusion reaction if the interval is greater than seven days after the sensitizing transfusion. Such reactions may vary from transient chills, fever, and jaundice to severe hemoglobinuria and anuria. In any case, no benefit is derived from the transfusion and some degree of harm results.

Subgroups<sup>11</sup> have been demonstrated among Rh-positive subjects so that an Rh-positive patient may be sensitized by a transfusion of Rh-positive blood of a different subgroup. Subsequent transfusion from the same donor to the same recipient then may cause a reaction, although this is a clinical rarity; the lesser subgroups make up only about 2.5 per cent of the total. Three different agglutinogens or antigenic factors ( $Rh_0$ ,  $Rh_{11}$ , and  $Rh_a$ ) which may be present in Rh-positive red blood cells are recognized at present; in combination with the corresponding serum types and the Rh-negative ( $rh$ ) type, this permits classification of human blood into eight different types with respect to Rh factor. Of these types,  $Rh_{11}$ ,  $Rh_a$ ,  $Rh_1Rh_a$  and  $rh$ , must be considered as Rh-negative with respect to the recipient of a transfusion or the obstetric patient. Such patients should receive transfusions of  $rh$  (true Rh negative) blood only, to prevent sensitization.

Rh-negative women married to Rh-positive men will sometimes develop anti-Rh agglutinins as a result of pregnancy<sup>13</sup> with an Rh-positive fetus. Although the first child is likely to be normal, the second child, if also Rh positive, may suffer a variable degree of hemolysis as a result of passage of the mother's anti-Rh

serum agglutinins across the placenta. The resulting damage to the child's red cells may cause injury varying from moderate jaundice and anemia to fatal erythroblastosis fetalis. In the most severe cases, when the maternal anti-Rh immunity is high, death of the fetus may occur at any time from the seventh month of development to the time of birth. In such a case, if the father is homozygous Rh positive, all his children will be Rh positive and are unlikely to survive. If he is heterozygous Rh positive, he may be fortunate enough to have an Rh-negative child, in which case a normal offspring will result. There is at present no way to alter these circumstances. The best that can be done is to make sure that no Rh-positive transfusion, either of whole blood or of suspended red cells, is given to an Rh-negative woman of child-bearing age. If a transfusion is needed in an Rh-negative young woman, blood from an Rh-negative donor always should be used. Although theoretically erythroblastosis should be common, the normal impermeability of the placenta is so high that serious pathologic change occurs only occasionally.

Patients who are likely to require several transfusions, patients who give a history of previous transfusion reactions, or patients who are young women in the child-bearing period should be typed to determine the Rh blood group before a transfusion is given. An Rh-negative patient of any of these classes should be transfused with Rh-negative blood only. This is especially important if the first transfusion is to be given during or immediately after operation,<sup>12</sup> when the patient is unable to complain and a reaction may occur unidentified.

A satisfactory rapid slide test for determination of Rh blood type has been described by Tisdall and Garland.<sup>14</sup> These authors made use of an anti-Rh testing serum containing agglutinins both for the major Rh-positive blood type and for one of the Rh-positive subgroups, so that the test gave a false negative response in only 0.5 per cent of Rh-positive bloods. Commercially available sera are chiefly of the type which agglutinate only the cells of the major Rh-positive group (Rh<sub>0</sub>), so that from 2.0 to 2.5 per cent of Rh-positive unknown bloods (subgroups) will give a false negative reaction.

The test as described makes use of a very thick cell suspension of the unknown blood, one drop of which is placed on a slide and mixed with one drop of anti-Rh testing serum. The resulting

suspension is mixed with a glass rod or with the bottom of a Kahn tube. Control tests also are set up with a known Rh-negative blood and a known Rh-positive blood for comparison with the test of the unknown specimen. The cell mixtures are allowed to rest for one minute, after which the slide is rotated once or twice to loosen the cells from the glass surface. The test is read when the known Rh-positive blood shows agglutination, which usually occurs within a minute. A positive reaction is evidenced by the appearance of macroscopic red granular clumps of agglutinated cells; microscopic examination is not necessary. By this technique, if the cells do not show agglutination within two minutes, the unknown blood is considered Rh negative. It is suggested that both the blood and the antiserum be at room temperature when used and that the unknown blood sample be less than twenty-four hours old.

With the commercial anti-Rh testing sera now available, slight differences in technique may be employed. For preparation of the cell suspension, two full drops of blood are mixed with 0.5 c.c. of normal salt solution in a Kahn tube to obtain a 10 per cent cell suspension. A thinner cell suspension may give a false negative reading. A small drop of anti-Rh serum is mixed on a slide with a similar drop of unknown cell suspension and is allowed to remain undisturbed for three minutes. During the next three-minute period, the slide is held above a source of light and is inspected constantly. Agglutination is evidenced by the appearance of fine red granules. Microscopic examination is not advisable nor should the test mixture be allowed to stand for more than six minutes before it is read. Control tests with known Rh-positive and known Rh-negative bloods are set up for comparison with the unknown.

The test tube technique for Rh typing takes a longer time. A 2 per cent cell suspension is made from the unknown blood and a drop of this suspension is mixed with a drop of known testing serum in a Kahn tube. The mixture is shaken and is incubated in a water bath at 37° C. for an hour. Control tests are set up in a similar manner. The tubes are balanced in a centrifuge and are spun at 1,000 r.p.m. for one and one-half minutes. The tubes are removed, shaken gently, and examined immediately for macroscopic agglutination. If necessary, a drop of the suspension is examined both macroscopically and microscopically on a clean

slide. The presence of agglutination indicates that the unknown blood is Rh positive. Complete typing can be done by use of known sera of the different types.

Demonstration of Rh sensitization is somewhat complicated by the fact that "blocking antibodies" as well as agglutinins may be present in sensitized serum and may interfere with agglutination. It is believed that these blocking substances are protein in nature<sup>15</sup> and produce their effect by forming a layer or coating over the Rh-positive red cells, used for testing, preventing agglutination by the anti-Rh serum agglutinins. A substance present in plasma ("conglutinin") is thought to be necessary to permit agglutination in the presence of blocking antibodies; this substance is inactivated by addition of water solutions of crystalloids. The blocking effect can be minimized therefore by the use of AB plasma (obtained from bank blood) instead of normal salt solution for the known Rh-positive cell suspension and for dilution of the unknown serum. As a rule, however, the blocking effect is not noticeable if the titer of the anti-Rh testing serum is high.

Unger and associates<sup>16</sup> suggest the routine testing of all donors and recipients for Rh group as well as for Moss group, advising the use of the more easily obtained testing serum containing pure anti-Rh<sub>0</sub> blocking antibodies, which will produce clumping in Rh<sub>0</sub>-positive blood (about 85 per cent of people). If no clumping occurs, the cells do not belong to the preponderant Rh<sub>0</sub>-positive group and therefore should be typed completely with Rh<sub>0</sub>, Rh<sub>+</sub>, and Rh<sub>++</sub> sera; if there is no agglutination with any of these testing sera, the blood is Rh negative. By this procedure, complete identification of Rh type can be made with a minimum of testing; it is advocated by these authors as being particularly applicable to the operation of a blood bank.

### Methods of Blood Transfusion

The many techniques for administering blood transfusions differ in minor details but can be classified into two broad groups. In the direct method untreated blood is transferred from donor to recipient rapidly and by such a technique that the transfer is completed before the blood begins to clot. The indirect method involves the use of an anticoagulant, usually sodium citrate.

Transfusion by the *direct method* has never attained much popularity because of several serious disadvantages. Considerable dexterity and experience are necessary to assure the rapid and smooth conduct of the procedure; if clotting begins to occur, the transfusion must be discontinued at once. The recipient, especially if very ill or of a nervous temperament, is likely to become disturbed and excited by the fact that the donor is lying beside him and by the manipulations necessary to carry out the transfer of the blood. Finally, the apparatus required for direct transfusion is usually more costly than that necessary for the indirect method.

The simplest form of the direct method in principle involves the use of separate syringes for alternate rapid withdrawal and injection of the blood and requires a team of three people, with scrubbed hands and sterile gloves. An intravenous needle is inserted into a suitable vein in a sterile field in the recipient's arm and another is similarly placed in the donor's arm. One member of the team withdraws 50 c.c. of blood from the donor's vein and passes the syringe to another member of the team, who injects the blood into the recipient's vein. A third person washes the syringe after use in a sterile solution of sodium citrate (2 per cent) or in normal salt solution. If at least four syringes are used and if the needles are not withdrawn from the veins, the procedure may be made a continuous one, although clotting is very likely to occur.

Other methods of direct transfusion include the Kimpton-Brown paraffined tubes, the Jubé apparatus, and the DeBakey apparatus,<sup>4</sup> all of which require familiarity with the apparatus and a certain degree of dexterity. The latter two methods permit withdrawal of blood from the donor and administration to the recipient almost simultaneously. Care must be taken with these devices that the flow proceeds in the proper direction; it is possible to give the prospective donor a transfusion of the recipient's blood, which might produce a serious reaction in a donor (if, for example, type IV).

A compromise between the direct and indirect methods of transfusion was effected by Hedenius,<sup>17</sup> who obviated the disadvantages of indirect transfusion of citrated blood by heparinizing the donor. Heparin is administered intravenously to the donor in quantities of 1.0 to 1.25 mg. per kilogram of body weight. Ten minutes later the amount of blood desired is withdrawn from the

donor and transfused into the recipient by any technique desired. Coagulation of the drawn blood will not begin in less than one-half hour, but the transfusion must be completed within that time. The donor's blood will retain the heparin effect for about two hours; he should be kept at rest for that length of time and any possibility of injury avoided. The method of transfusion by heparinization of the donor will probably be of most value as an emergency method outside of hospitals, when standard transfusion equipment is not available, or as a preparation for the multiple syringe method of transfusion.

The *indirect method*, in which an anticoagulant is added to the blood as it is collected, is the most widely preferred. By this procedure the blood can be collected from the donor in a laboratory and transfused later into the recipient as slowly and as simply as an ordinary infusion is given. There is no need for haste, and the blood may be given after several days, if necessary, provided it is kept in the icebox during the interval. The patient is relieved of the necessity of enduring the bustle and unpleasantness that usually accompany a direct transfusion, during which the donor lies beside the recipient; in fact, if the indirect method is used, the patient may even be unaware that blood, rather than dextrose solution, is being administered. The method is a simple one and the procedure can be performed with no difficulty, even with little previous experience.

One of the greatest advantages of the indirect method is that a small amount of blood may be introduced into the recipient's vein and then the flow may be stopped until the presence or absence of a transfusion reaction can be determined. This is not possible when the direct method is used.

### Collection of Blood

Although a great many hospitals now use commercially prepared transfusion bottles and apparatus, many still employ their own blood collection and transfusion systems. These individual methods differ slightly in details but the principle of operation is in general much the same. The method described below is probably typical in most respects. The use of commercial transfusion apparatus is described in the Appendix.



After the collecting set has been assembled (Fig. 11), 10 c.c. of sterile sodium citrate solution (2.5 per cent) for each 100 c.c. of blood to be collected is aspirated through the needle. The small amount of anticoagulant used has no effect on the recipient's clotting time, even when pathologically increased, for there is always sufficient serum calcium to combine with it. This is true

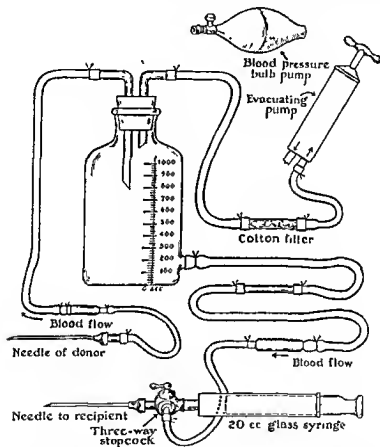


Fig. 11 —Apparatus for blood transfusion, indirect method. Anticoagulant solution is drawn into the collecting flask, and blood is then drawn from the donor. The outflow apparatus is assembled and attached to the outlet tube, which has been kept clamped up to this time. If the inflow tube is clamped near the bottle, and the suction pump replaced by a force bulb, the transfusion can be given rapidly. A filter and drip chamber (not shown) should be used. If the stopper assembly is removed and the open top of the flask covered by an inverted medicine glass, the transfusion can be given by gravity. Apparatus of this type, formerly in wide use, is being replaced generally by commercially prepared transfusion equipment. (Appendix, p 812).

even in jaundiced patients, transfusions of citrated blood being as valuable as transfusions of untreated blood. It is possible that the use of the chemical may increase somewhat the incidence of mild transfusion reactions, but this effect is of little real importance.

It is probably best to have the donor lying down, in case he should faint. A tourniquet, preferably a sphygmomanometer cuff,

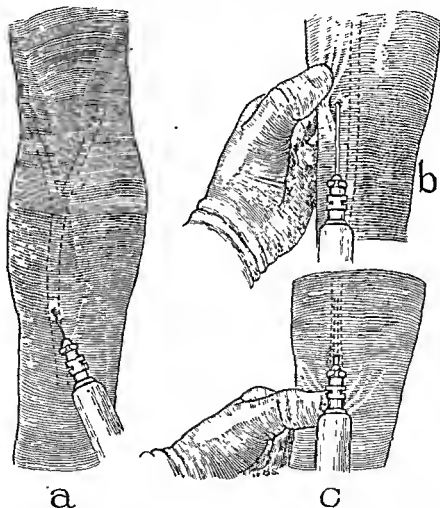


Fig 12—Venipuncture with a large needle. *a*. A wheal of procaine (0.5 per cent) is made with a small hypodermic needle at the proposed site of puncture. *b*. The skin is drawn to one side of the vein and the large needle inserted through the wheal. *c*. The skin over the vein is drawn downward and fixed with the left thumb to prevent the vein from rolling away during venipuncture.

is applied to the donor's upper arm but is not yet tightened. The operator, who has previously prepared his hands as for a surgical operation and has put on sterile gloves, then cleans the skin over the donor's selected vein with two coats of iodine and alcohol, the iodine being allowed to dry before removal. Sterile towels are placed around the area. The spot to be punctured is pulled a little to one side and a wheal of procaine (1 per cent) injected, after which the injected area is allowed to slide back to its original position above the vein (Fig. 12). The tourniquet is tightened by an assistant, and the venipuncture is carefully performed with a large (16 to 18 gauge) needle. In most cases, it is advisable to make a small nick in the skin with a scalpel before attempting to introduce the needle. Gentle suction is applied. If no blood is obtained, very slight withdrawal of the needle may help; both sides of the vein may have been pierced or the vessel wall may have been drawn against the beveled edge of the needle by the suction. The pump is used just enough to keep the blood flowing in a steady stream; too much suction may cause an entire segment of the vein to collapse. Rhythmical slow flexion of the donor's fingers will increase the rate of blood flow. The bottle is agitated slowly and constantly by an assistant to insure thorough mixing of the blood with the citrate solution. An additional amount of blood equal to the amount of citrate used is drawn to allow for volume of anticoagulant.

### Administration of Blood

If the collecting bottle is provided with an outlet near the bottom (Fig. 11), the blood may be introduced into the recipient's selected vein through a tube and needle attached to the outlet. If not, the stopper should be removed, the lip flamed, and the blood poured through a sterile funnel into the bottle of an ordinary intravenous set which can be used for administering the transfusion. The blood should be filtered through a sterile filter as an intermediate step. In the set illustrated, when collection is complete, a small quantity of sterile normal salt solution is aspirated through the needle to clean the tube, which is then clamped shut. The suction bulb is replaced with a pressure bulb and a sterile needle is attached to the outflow tube. The tubing is filled with blood slowly by gentle pressure on the

bulb to remove the air. The transfusion is administered slowly to the recipient, through a medium needle (18 to 19 gauge).

Except in emergencies, blood is given slowly, at a rate of from 50 to 60 drops per minute. After 50 c.c. has been administered at this rate, the rate of flow is cut down temporarily and the patient watched for signs of a possible reaction, such as nervousness, tachycardia, pallor, sweating, headache, nausea, chill, or pain in the lumbar region or extremities. If any of these signs is observed, the transfusion is immediately discontinued and epinephrine, 0.5 to 1.0 c.c. (1:1,000), administered. Otherwise,

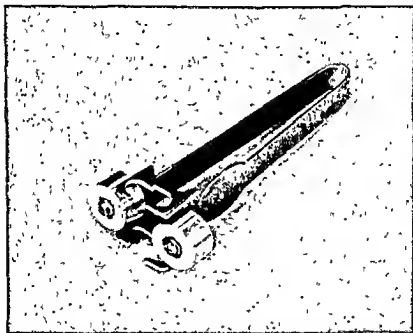


Fig. 13 —Hand roller for the rapid intravenous administration of solutions (From Lundy and Rogers Proc. Staff Meet., Mayo Clin 13: 726, 1938)

the blood may be given slowly until the transfusion is completed, administration of 500 c.c. requiring about two hours. An attendant should remain constantly in the room with a patient receiving a blood transfusion. Sometimes administration by gravity or by pressure pump does not permit a sufficiently rapid introduction of blood or fluid in patients needing it urgently. Progressive compression of the rubber tubing by hand or by some form of hand roller, such as the instrument (Figs. 13 and 14)

devised by Lundy and Rogers,<sup>18</sup> will increase the speed of flow of the intravenous injection. These authors state that 500 c c of blood can be transfused when necessary in less than five minutes by the use of their instrument.



Fig. 14—Hand roller in place on tube. Position of hands shown. (From Lundy and Rogers. *Proc. Staff Meet., Mayo Clin* 12: 727, 1938.)

Although definitely not an acceptable method, blood for an indirect transfusion may be collected in an emergency when no set is available by applying a tourniquet to the donor's arm, cleaning the area to be punctured, inserting, under complete aseptic precautions, a fairly large needle with a sterile tube attached, and allowing the blood to drop directly into a sterile wide-mouthed container holding the requisite amount of citrate solution. Following collection and proper mixing with the citrate

solution, the blood is administered in the usual manner by means of a transfusion set equipped with a satisfactory sterile filter. About 100 c.c. of normal salt solution should be poured into the intravenous set and allowed to start running into the vein before the blood is added. More detailed information concerning the technique of blood transfusion can be found in the books by Kilduffe and DeBakey<sup>4</sup> and by Wiener.<sup>19</sup>

The use of the intramedullary route for administration of blood transfusions has been suggested by Tocantins and O'Neill<sup>20</sup> and advocated also by many others following increased experience with the method. Intraosseous transfusions are not without some danger, however, and familiarity should be gained with the procedure before it is attempted. In general, it is more satisfactory for infusion of aqueous solutions than for transfusion of blood and is of particular value in the care of infants and small children (p. 44).

### Transfusion Reactions

Unremitting care of a high degree is necessary to prevent the occurrence of serious transfusion reactions. The selection of the proper donors and the collection and administration of blood to the patient are not complicated procedures and they are well handled by any capable intern. On the other hand, there is no margin for the least error or carelessness in any step of the process; a fatal hemolytic reaction may occur suddenly and with little warning if incompatible blood is administered. Minor reactions, which may cause further injury to an already ill patient, result from the use of improperly cleaned apparatus, impure anticoagulant solutions, or bank blood contaminated during collection or storage. Finally, various diseases may be transmitted through blood transfusions if the precaution of investigating the donor beforehand is not taken. Well-authenticated instances have been reported of the transmission by transfusion of malaria, syphilis, and various virus diseases such as infectious hepatitis.

**Hemolytic Reactions.**—Reactions due to transfusion of incompatible blood are no longer common because of the well-planned routine for collection and administration of blood in all hospitals. This complication of blood transfusion, the most

dangerous one, is due to agglutination and lysis of the donor's red blood cells by specific agglutinins in the recipient's serum, with the release of products of the hemolysis into the blood stream.

If incompatible blood is unwittingly administered, the resulting reaction usually is immediate and profound. After perhaps 50 c.c. of incompatible blood has been introduced, the patient typically develops a feeling of fullness or bursting in the head, severe pain in the lower back, and a sensation of constriction of the chest with marked dyspnea. Nausea and vomiting may appear, with such signs of progressive vascular collapse as a rapid soft pulse and a sudden drop in blood pressure. Within a short time, the temperature rises rapidly and a severe chill develops. If the transfusion is discontinued at the first sign of a reaction, the adverse symptoms continue for a few minutes and then gradually disappear. Continuance of the transfusion, however, causes a rapid development of irreversible shock and sometimes sudden death.

After subsidence of the acute symptoms, the patient usually recovers rapidly and has no complaints. Within a few hours, hemoglobinuria develops and the urine shows positive tests for blood and albumin. If the reaction is mild, transient oliguria develops, from which recovery is rapid and complete. More severe reactions are followed, after several days of apparently normal health, by jaundice, progressive oliguria, and finally death in uremia. Death following transfusion of incompatible blood therefore may result either immediately from shock or within a week or more from secondary renal insufficiency.

The over-all mortality rate for hemolytic reactions due to transfusion of incompatible blood is at least 50 per cent, the prognosis of each individual case depending upon the size of the transfusion and the general health of the patient. As a rule, patients who have received less than 100 c.c. of incompatible blood will recover, while similar transfusions of 250 to 500 c.c. will almost always produce a fatal reaction, especially if the patient is already weakened by anemia or coincident visceral disease.

The cause of renal failure following severe transfusion reactions has never been established. Various explanations have been proposed, such as blockage of the renal tubules by hemoglobin precipitated in an acid urine, occurrence of a substance in the

hemolyzed blood toxic to the kidneys, and temporary vascular spasm throughout the kidneys with permanent damage resulting. At necropsy, the kidney is distended and pale, with microscopically normal glomeruli, interstitial edema, dilated proximal convoluted tubules, and necrosis of epithelium in the distal tubules.<sup>21</sup> The theory postulating the presence of a nephrotoxic substance in the hemolyzed blood probably is the most plausible.

Hemolytic reactions due to Rh incompatibility are milder than those due to group incompatibility, but are similar otherwise. If the cause of the reaction is not recognized and more transfusions of the same nature are given, succeeding reactions become more severe and may be fatal.

Transfusion of bank blood that has been stored for more than seven to ten days may be followed by rapid hemolysis of a large percentage of the transfused cells even though no incompatibility is present. Hemolysis of this type usually produces only a mild reaction if any, although slight transient jaundice may appear.

**TREATMENT.**—Treatment of hemolytic reactions offers very little help but should be instituted at once. The first 50 c.c. of a transfusion always is given slowly, at a rate not exceeding 60 drops per minute, with an attendant present to watch for evidence of a reaction. If untoward signs appear or if the patient complains of headache, nausea, or backache, the transfusion is discontinued instantly and the unused blood is returned to the laboratory for verification of the cross matching. Epinephrine (1:1,000) is administered in doses of 0.5 to 1.0 c.c., and blankets are supplied if a chill develops. Impending or actual shock may require administration of plasma or of another more carefully matched blood transfusion.

The only other worth-while procedure is the administration of alkalis. Preliminary alkalization has been suggested by DeGowin<sup>22</sup> and others as a routine prophylactic measure before all transfusions to minimize the precipitation of hemoglobin in the kidneys in case a hemolytic reaction should occur. This measure has not yet been widely adopted, but administration of alkali in treatment of such reactions is well recognized. Alkalization probably is useless after a reaction has occurred, because the damage already has been done. Oral administration of alkali is of little value; absorption is too slow and the amount



required is too variable. Rapid alkalinizing of the urine is accomplished best by intravenous injection of sterile one-sixth molar sodium r-lactate solution (18.66 Gm. of sodium r-lactate per liter) in a dose of 500 c.c., repeated after several hours if necessary. Sodium bicarbonate, prepared and sterilized in the hospital, may be too strongly alkaline for intravenous use because of partial transformation into sodium carbonate. Commercially prepared sealed ampules of sodium bicarbonate (4 per cent) are available and are safer. This solution usually is given intravenously in quantities of 300 c.c. administered very slowly.

When anuria develops, measures are taken to stimulate urinary output. Intravenous injection of 1,000 c.c. of 10 to 20 per cent dextrose or of 50 to 100 c.c. of 50 per cent dextrose may be worth trial. Renal decapsulation has been advocated<sup>46</sup> and is worth trying if medical methods fail (p. 281).

**Pyrogenic Reactions.**—Mild transfusion reactions are relatively frequent and consist simply of a transitory rise in temperature of from 2 to 6° F. Various mild systemic symptoms such as headache, nausea, weakness, palpitation, lumbar pain, or rigor may be present. No specific treatment is necessary; application of extra blankets may add to the patient's comfort and warm drinks usually are appreciated. Administration of epinephrine, 0.5 to 1.0 c.c. (1:1,000) hypodermically, or of morphine, 10 to 16 mg. (gr. 1/6 to 1/4) hypodermically, will relieve the discomfort. Symptoms of this type do not often persist for more than an hour or two.

Pyrogenic reactions follow the use of improperly prepared anticoagulant or preservative solutions or of improperly cleaned apparatus. Several observers have felt that the relatively large amount of citrate (anticoagulant) administered with massive transfusions produces toxic affects, but this has not been confirmed and the consensus is that such reactions are due to other causes.

The by-products of bacterial growth and decomposition present in tap water or arising from contamination of apparatus improperly cleaned after use will produce a febrile reaction and a chill if injected intravenously into a patient. Such pyrogens are uniformly present in tap water and can be completely removed only by triple distillation. Pyrogens also arise from bacterial

growth if flasks, stoppers, tubing, and needles stained with blood or crystalloid solutions are put aside for several hours before cleaning or are washed with tap water and allowed to stand for several hours before sterilization. Rigorous attention to detail is necessary in the preparation of solutions and apparatus for use in collecting or transfusing blood.

**Allergic Reactions.**—Allergic reactions to blood transfusion usually appear simply as transient urticaria but occasionally are severe, with asthma or angioneurotic edema. Such complications probably are due to reactions of the recipient to specific allergens contained in the donor's blood, for example, to certain foods. For this reason, fasting donors are preferred and, more particularly, donors who show no allergic sensitizations.

Any evidence of allergen transfer requires immediate discontinuance of the transfusion. Epinephrine (1:1,000), 0.3 to 0.8 c.c. hypodermically, will produce a prompt disappearance of the reaction. Benadryl, 50 to 100 mg., or Pyribenzamine, 50 mg., also will relieve acute allergic urticaria of this type. The dose may be repeated after several hours if necessary.

### Blood Banks

The facts that compatible donors may be difficult to find and that withdrawal and preparation of blood for transfusion require considerable time have led to the establishment at many hospitals of banks or stores of blood for transfusion, classified according to type and date of collection.

Methods of collection and preservation are becoming more or less standardized. The management of the blood bank at the Massachusetts General Hospital has been described in detail by Soutter<sup>24</sup>; the system and technique used at that hospital probably are typical of the average well-managed hospital blood bank.

Some institutions secure blood for transfusion from sources other than healthy living individuals. In Russia, Yudin<sup>25</sup> and associates have developed a large blood bank, using blood secured from undamaged cadavers within six hours after death. Sufficient quantities of suitable blood probably would be difficult to obtain except in the largest population centers, and the esthetic acceptability of the procedure is by no means universal. Placental

blood,<sup>16</sup> collected under sterile precautions from healthy subjects at the time of delivery, has been used to supply blood banks at various centers in this country, but again there are too many disadvantages for the method to have wide appeal.

During World War II many thousands of liters of blood were drawn from healthy donors at the American Red Cross centers throughout the United States. The red cells were separated and the plasma was desiccated, stored in sterile units, and sent overseas for use by the Armed Forces. In many instances, the fresh discarded red cells were resuspended in an amount of sterile normal salt solution equal to or less than the removed plasma and were used as transfusions in place of whole blood at various hospitals. Reports that have been made on the use of red blood cell suspensions indicate that they are satisfactory in the treatment of anemia, although considerably less satisfactory in the treatment of other conditions requiring whole blood transfusion. Careful cross matching of the red blood cell suspension against the recipient's blood is necessary, just as in an ordinary blood transfusion. The only indication for administration of red cell-saline suspension at present is anemia with normal plasma protein concentration. The chief advantage is that an excellent use is found for the red cells formerly discarded as a by-product in the preparation and preservation of plasma. Red blood cells that are discarded from bank blood cannot be used for transfusion by any method; such cells are over age and are unfit for introduction into the circulating blood. The use of red blood cells for administration in suspension in normal salt solution is restricted to freshly drawn cells, discarded during processing of plasma. Thalhimer and Taylor<sup>27</sup> have described a satisfactory method of preserving, utilizing, and administering red blood cell transfusions, using a sterile solution of 10 per cent corn syrup in distilled water as a preservative and vehicle. The survival of red blood cells preserved in this manner and stored is approximately the same as that of the red blood cells in whole bank blood.

Despite the obvious advantages of the blood bank, there are certain factors which render stored whole blood somewhat inferior to fresh blood for transfusion. Autolytic changes take place in refrigerated blood, which is preserved best under aseptic precautions within a temperature range of 0 to 5° C. Although very little actual hemolysis takes place for nearly two weeks after the

blood has been collected, the fragility of the red cells increases with the length of preservation. The flasks containing blood should be handled gently; agitation increases the tendency of the cells to hemolysis and decreases the length of time such blood may be stored safely before use. Exposure to air also increases the fragility of the cells; flasks containing stored blood may be filled completely, with total exclusion of air, or the blood may be stored in a vacuum flask. The blood transfusion field service of the United States Army, which supplied great quantities of whole blood to field and evacuation hospitals during World War II, made a practice of filling the flasks completely to minimize exposure to air and to decrease the tendency to agitation of the blood within the flask during transportation.

Normally, erythrocytes remain in the circulating blood for a period of three to four months; this is true also of the red cells in blood which is transfused immediately after collection or, to a lesser degree, within five days after withdrawal. Blood which has been preserved for more than ten days usually is not of much value to the recipient and sometimes may do actual harm; rapid hemolysis of the transfused erythrocytes may take place and hemoglobinuria and transfusion reactions of varying degrees of severity may occur. The red cells in blood preserved for such a long time do not remain in the recipient's blood stream for more than a few days before they break down, and an icteric tint sometimes can be observed in the patient's serum at this time. In general, the optimum safe limit for storage of preserved blood is about five days or, at most, seven days. After this time, the cells can be separated and discarded and the plasma preserved either by desiccation or as a liquid.

Alterations occur in other constituents of conserved blood. A shift of potassium ions from the erythrocytes to the plasma has been demonstrated by Scudder and co-workers,<sup>28</sup> who feel that blood preserved for more than five days may be somewhat toxic when transfused, as a result of the increased plasma potassium.

The prothrombin content of conserved blood decreases very rapidly, as shown by Rhoads and Panzer,<sup>29</sup> so that blood preserved for even two or three days cannot be used to combat the bleeding tendency due to prothrombin deficiency, as in obstructive jaundice. Although other investigators have extended this period somewhat, it is universally agreed that there is a significant drop

in prothrombin concentration of preserved blood after the first few days of storage. Freshly drawn blood should therefore be used for this purpose.

Within these limitations preserved blood has been demonstrated to be safe for transfusion and has gained wide acceptance as a substitute for the less readily available fresh blood.

### References

1. Crook, C. L., Ioh, V., and Collier, F. A.: Correction of Blood Loss During Surgical Operations, *Surg., Gynec. & Obst.* 82: 417, 1946.
2. Witebsky, E., Klendshoj, N., and Swanson, P.: Preparation and Transfusion of Safe Universal Blood, *J. A. M. A.* 116: 2654, 1941.
3. Klendshoj, N. C., and Witebsky, E.: Transfusion of O Blood Conditioned by Addition of Blood Group-Specific Substances; Further Clinical Investigation, *J. A. M. A.* 128: 1091, 1945.
4. Kilduffe, R. A., and DeBaakey, M. E.: *Blood Bank and the Technique and Therapeutics of Transfusion*, St. Louis, 1942, The C. V. Mosby Co.
5. Stats, D., and Wasserman, L. R.: Cold Hemagglutination: An Interpretative Review, *Medicine* 22: 363, 1943.
6. Dameshek, W.: Cold Agglutinins in Acute Hemolytic Reactions in Association With Sulfonamide Medication and Infection, *J. A. M. A.* 123: 77, 1943.
7. Dameshek, W.: Medical Progress; Hematology, *New England J. Med.* 230: 514, 542, 1944.
8. Lever, W. F., and Massie, W. K.: The Laughlen Test in the Diagnosis of Syphilis, *Arch. Dermat. & Syph.* 40: 45, 1939.
9. Landsteiner, K., and Wiener, A. S.: Agglutinable Factor in Human Blood Recognized by Immune Sera for Rhesus Blood, *Proc. Soc. Exper. Biol. & Med.* 43: 223, 1940.
10. Wiener, A. S.: Heredity of Rh Blood Types, *J. Exper. Med.* 79: 235, 1944.
11. Levine, P.: Present Status of the Rh Factor, *Am. J. Clin. Path.* 16: 597, 1946.
12. Diamond, L. K.: Medical Progress; Clinical Importance of Rh Blood Type, *New England J. Med.* 232: 447, 475, 1945.
13. Potter, E. L.: Present Status of Rh Factor, *Am. J. Dis. Child* 68: 32, 1944.
14. Tisdall, L. H., and Garland, D. M.: Large Scale Testing for Rh Negative Blood, *J. A. M. A.* 129: 1079, 1945.
15. Wiener, A. S.: Recent Developments in the Knowledge of the Rh-Hr Blood Types; Tests for Rh Sensitization, *Am. J. Clin. Path.* 16: 477, 1946.
16. Unger, L. J., Weinberg, M., and Lefkowitz, M.: The Rh Factor as Applied to the Operation of Blood Banks, *Am. J. Clin. Path.* 16: 498, 1946.

17. Hedenius, P.: Further Experience With Heparinising the Donor in Blood Transfusions, *Lancet* 2: 1186, 1937.
18. Lundy, J. S., and Rogers, D. A.: Hand-Roller for Rapid, Intravenous Administration of Urgently Needed Blood or Solutions, *Proc. Staff Meet., Mayo Clin.* 13: 726, 1938.
19. Wiener, A. S.: *Blood Groups and Transfusion*, ed. 3, Springfield, Ill., 1943, Charles C Thomas.
20. Tocantins, L. M., and O'Neill, J. F.: Complications of Intra Osseous Therapy, *Ann. Surg.* 122: 266, 1945.
21. DeGowin, E. L., Warner, E. D., and Randall, W. L.: Renal Insufficiency From Blood Transfusion; Anatomic Changes in Man Compared With Those in Dogs With Experimental Hemoglobinuria, *Arch. Int. Med.* 61: 609, 1938.
22. DeGowin, E. L.: Grave Sequelae of Blood Transfusion; Clinical Study of 13 Cases Occurring in 3,500 Blood Transfusions, *Ann. Int. Med.* 11: 1777, 1938.
23. Lyons, J. H., and Raines, S. L.: Renal Decapsulation for Transfusion Oliguria, *Ann. Surg.* 122: 894, 1945.
24. Soutter, L.: Procedures of Blood Bank at Massachusetts General Hospital, *New England J. Med.* 230: 157, 1944.
25. Yudin, S. S.: Transfusion of Cadaver Blood, *J. A. M. A.* 106: 997, 1936.
26. Barton, F. E., and Hearne, J. M.: The Use of Placental Blood for Transfusion, *J. A. M. A.* 113: 1475, 1939.
27. Thalheimer, W., and Taylor, E. S.: Transfusion of Centrifuged Human Type O Cells Resuspended and Stored in 10 Per Cent Corn Syrup, *J. A. M. A.* 127: 1096, 1945.
28. Scudder, J., Drewe, C. R., Corcoran, D. R., and Bull, D. C.: Studies in Blood Preservation 1. Repartition of Potassium in Cells and Plasma, *J. A. M. A.* 112: 2263, 1939.
29. Rhoads, J. E., and Panzer, L. M.: Prothrombin Time of "Bank Blood," *J. A. M. A.* 112: 309, 1939.

## CHAPTER 9

### SYSTEMIC COMPLICATING FACTORS

Certain unrelated pathologic conditions coexisting in a patient in need of surgery may require special preparation and aftercare. Examination will readily disclose any of the common complications that may be present and often simple precautionary measures may transform a poor operative risk into a good one.

#### Extremes of Age

Patients in the extremes of life are generally subject to a higher operative mortality and morbidity than are other subjects, although proper care will usually reduce the risk to a point at which surgery can be undertaken without undue worry. Children, especially under 1 year of age, and old people, especially over 70 years of age, present particular problems.

**Infants and Young Children.**—Infants and young children normally have a much higher metabolic rate than adults and are unusually susceptible to physiologic disturbances. Any factor that reduces the food intake or any significant infection will rapidly produce a depletion of body fluids and of stored glycogen. Vomiting, for example, either as a result of systemic disease or of gastrointestinal obstruction not only will prevent proper food intake and glycogen deposition, but also will produce dehydration and loss of body chlorides. The resulting electrolyte imbalance sometimes is so marked that tetany may result. In a child, diarrhea with its general debilitating effect and drainage of body fluids may also produce rapid dehydration and a high temperature within a very short time. Either vomiting or diarrhea may interfere so greatly with nutrition that starvation acidosis will develop from increased metabolic oxidation of body fat in the absence of sufficient carbohydrates. Such physiologic disturbances as vomiting and diarrhea in patients of this age group should be accorded their true importance and the consequent fluid and electrolyte losses should be corrected immediately.

Care of the child throughout the entire preoperative and postoperative course must be divided between a qualified

pediatrician and the surgeon. The child is not simply a small adult; management of patients in this age group requires such specialized knowledge that a pediatrician's services are indispensable. The surgeon, however, must recognize certain definite problems peculiar to the care of children.

Psychic trauma inflicted upon a child by his stay in a hospital and particularly by a surgical procedure may produce subsequent behavior problems and fears that will prove difficult to eradicate. Some simple explanation of the necessity for hospitalization and operation should be given to the child, and a near relative, preferably his mother, should accompany him and be present when he meets those who will care for him. Efforts of the attendants to establish friendly relations with the suspicious and terrified patient will save a great deal of time later if a cooperative frame of mind can be induced. Children may fear the dark in unfamiliar surroundings, and a night light in the room may be necessary. A small dose of barbiturate elixir on the first night is useful. Most important of all is the fact that the child should not be brought to the operating room while fully conscious to wait for some time before induction of anesthesia. The picture of a wildly terrified, screaming child fighting the anesthetist is still too often seen in hospital operating rooms and the effects of the experience on the patient's subsequent course and subsequent attitude should be self-evident. A child should always receive a sufficient dose of a barbiturate or of a basal anesthetic such as Avertin to induce sleep before he is taken from his room. It is highly advisable also for his mother to be present, so that he may feel secure when he falls asleep and again when he awakens after operation. A clear discussion<sup>1</sup> of this aspect of pediatric surgery has been written by Levy.

**PHYSICAL EXAMINATION.**—Complete physical examination must be performed with as much care as in the adult. Urine specimens are not routinely necessary but may be collected in infants, when desired, by tying a Pyrex test tube into a perineal binder and applying the binder so that the mouth of the tube is held firmly over the external urethral meatus. The infant should be watched closely to make sure that the tube does not break. Small infant urinals which are held entirely within the diaper can be obtained; these are more satisfactory, because there is no



danger of breakage and because urine may be collected no matter how the infant changes his position. Catheterization of an infant to secure a specimen of urine is difficult, dangerous, and unnecessary. Examination of the urine is always required in older children and the specimen is collected in the routine manner. The usual methods of securing blood for laboratory study are employed.

The extreme susceptibility of the child or infant to infection, especially of the respiratory tract, should be remembered. Any elevation of temperature, even of one degree, demands postponement of an elective operation until the cause of the fever can be determined and corrected. History of a beginning coryza or persisting cough prohibits all but emergency operations until the respiratory tract has been cleared of clinical infection. If visible reddening of the posterior pharynx or tonsillar areas is noted on examination, operation is deferred until after the presence or absence of an incipient pharyngitis has been decided. Especially in the winter or spring a day or two spent in the hospital before operation may permit the full development of an upper respiratory tract infection which has begun before admission but has not become clinically apparent. Too much care cannot be taken in this respect. The practice of bringing a child to the hospital on the morning of operation, or even on the night before, is a dangerous one. If an anesthetic is administered and operation is performed in the presence of such an undiscovered infection, the subsequent course of the disease is usually severe and protracted. Relatives suffering from common colds should not be permitted to visit the child, even if masks are worn, because of the marked susceptibility of the young surgical patient to such infections.

There has been much discussion about the role played by the thymus gland in the respiratory and circulatory difficulties of young children subjected to general anesthesia. It has become a practice in some clinics to secure a preanesthetic roentgenogram of the chest in such patients, although many authorities believe this measure to be an unnecessary one.

**PREOPERATIVE PREPARATION.**—*Preoperative intake of fluids and of carbohydrates must be kept at a high level, since children tend to develop postoperative acidosis rapidly as a result of starvation. Infants should be kept on their normal feeding*

schedules as long as possible, the last feeding usually being given two hours before operation. Older children may be given added amounts of sugar in the form of orange juice with lactose added, hard candy, and bread with jelly or syrup. The fluid intake must be watched and a glassful of water administered every hour or two while the patient is awake. Infants or children who are too ill to take sufficient food and fluid by mouth may be given fluids by hypodermoclysis or by infusion. Infusions ordinarily are used only in extremely ill infants, since venipuncture in a small child is not easy. If infusions are used, babies under 1 year of age are given up to 15 c.c. of 5 per cent dextrose per pound of body weight twice daily. The same amount of normal salt solution is given by hypodermoclysis in addition. When intravenous injection of fluids is unnecessary or is too difficult and oral administration is impossible, proper hydration may be effected by hypodermoclysis alone. Normal salt solution is generally used for subcutaneous injection since dextrose solutions may be irritating to the tissues. Dilute solutions of dextrose can be given by hypodermoclysis if necessary, however, either as 5 per cent solution in distilled water or as a mixture of 5 per cent dextrose and normal salt solutions in equal parts. If such injections are rotated between the subscapular regions, buttocks, and lateral thighs, up to 30 c.c. of fluid per pound body weight can be given twice daily. Although it is difficult to keep the infant's daily total fluid intake up to the optimum of 60 to 90 c.c. per pound per day unless fluids are taken by mouth, at least half this amount can be given parenterally without much difficulty. Intraosseous infusions (p. 44) are sometimes used but are not yet widely popular. Older children require somewhat less fluid in proportion to body weight.

Occasionally, undernourished or chronically ill infants may exhibit definite anemia. Preoperative preparation of such patients must include transfusions of whole blood, preferably in several divided doses rather than by one or two large transfusions. Not over 20 to 25 c.c. of blood per kilogram (10 c.c. per pound) body weight should be given at one time. Determinations of bleeding time and clotting time are indicated in small children, especially in infants. If a coagulation deficiency is present, the specific measures indicated are taken to replace the lacking factor (p. 218). Such replacement can be effected temporarily

most simply by means of a fresh whole blood transfusion. Vitamin B complex, vitamin C, and, in infants, vitamin K are given parenterally in therapeutic dosage proportionate to age and weight of the child.

Blood chemistry studies cannot be made in small infants without difficulty. In older children whose body fluids have been depleted by malnutrition, vomiting, or diarrhea, an estimation of the sugar, nonprotein nitrogen, chlorides, and carbon-dioxide combining power of the blood may afford useful information. If blood chemistry determinations are not possible, examination of the urine for the presence of ketone bodies may sometimes give evidence of acidosis, which, if present, must be corrected before operation, even if the surgical condition demands emergency treatment.

Donovan<sup>2</sup> and others report a mortality rate approximating 1 per cent or less in several large series of patients with congenital hypertrophic pyloric stenosis treated surgically and attribute the reduction in operative mortality chiefly to the improvement in preoperative care. This condition is no longer regarded as a surgical emergency; from three to five days may be spent in establishing a normal fluid and electrolyte balance in these dehydrated infants. Normal salt solution (either alone or with added dextrose solution) is given by hypodermoclysis in quantities of from 20 to 30 c.c. per pound of body weight twice daily together with 2 ounces of 5 per cent dextrose solution by mouth every three hours. Formula feedings, even thick formulas, are not completely absorbed by infants with severe pyloric stenosis and should not be used during the immediate preoperative period. Infusions of 10 per cent dextrose and transfusions of whole blood are only occasionally necessary in these patients. The striking reduction in the mortality rate of this operative procedure is sufficient evidence of the necessity for preoperative correction of disturbances in fluid and salt balance. It is advisable to introduce a small urethral catheter (8 to 10 French) into the stomach just before operation for pyloric stenosis and to lavage the stomach gently with warm dilute sodium chloride solution, so that chances of contamination will be at a minimum if perforation of the mucosa occurs during performance of the Fredet-Rammstedt procedure. The catheter is allowed to remain in the stomach during operation to permit aspiration of swallowed air

If a child who has been admitted for emergency operation has eaten solid food within the preceding two or three hours, he probably will vomit during induction of anesthesia. Under such circumstances, it may save time if gastric lavage is performed or if a gag is introduced into the pharynx as soon as the first stage of anesthesia is reached, so that the stomach may be emptied without further ado.

**POSTOPERATIVE CARE.**—Following operation, every effort should be made to conserve body heat, which children tend to lose rapidly because of their high average metabolic rate and their relatively large surface area. Warm, light blankets should be applied and well-wrapped hot-water bottles may be useful. On the other hand, excess covering and tight wrapping will interfere with elimination of moisture from the skin surface and will cause the baby to become hot, damp, and uncomfortable. Wet or damp clothing must be changed promptly. When possible, small infants should be kept in a room in which the temperature is constant. If the operation has been a serious one, the danger of shock must be considered, since loss of a very small amount of blood in a child is equivalent to a large hemorrhage in an adult because of the small total blood volume. If a tendency to development of shock is noted, an infusion of normal salt solution and dextrose (5 per cent) solution, in amounts up to 20 or 25 c.c. per kilogram of body weight, is given, and a blood transfusion is prepared. Rather than waste time and add trauma by unsuccessful attempts at venipuncture for transfusion in incipient shock, it is usually best to select a suitable superficial vein, expose it aseptically by an oblique incision 1 cm. long, and obtain a satisfactory insertion of the needle on the first attempt.

Special attention must be paid to the maintenance of an adequate fluid and carbohydrate intake during the immediate postoperative period. Infants, for example after a Fredet-Ramstedt procedure for pyloric stenosis, may be given fluids by mouth within six to eight hours after operation and the feeding schedule gradually increased to 30 c.c. every three hours by the second day and to normal by the sixth day. For the first two or three feedings, small amounts of dextrose solution (5 per cent) alone is probably best, with breast milk or formula diluted with equal parts of water for the succeeding twenty-four hours.

and then undiluted breast milk or formula in gradually increasing amounts. Donovan<sup>2</sup> advises administration of feedings by medicine dropper for the first five days after operation and suggests that the head of the bed be elevated 20 degrees during feeding but that the infant not be picked up. Additional fluid is supplied by hypodermoclysis during the first three days.

If vomiting occurs in infants following any surgical procedure, a small stomach tube (8 to 10 French) may be inserted and gastric lavage performed. Care should always be taken that the tube does not accidentally enter the trachea. In any case, if sufficient fluid is not taken by mouth, the proper quantities of normal salt and dilute dextrose solutions should be given by hypodermoclysis. When vomiting ceases, oral feeding is begun with dextrose solution, followed by milk formula in increasing strength. Medical and dietary management of infants must always be supervised by a pediatrician, but it is of the greatest importance for the surgeon to recognize the need for maintenance of a proper fluid and electrolyte balance.

As a rule, the operative area is protected with a waterproof adhesive or collodion dressing to avoid excretory contamination and it may sometimes be necessary to bandage light pasteboard splints along the infant's arms to prevent him from scratching at the dressing. Skin reactions to zinc oxide adhesive tape are common in children; collodion may be more satisfactory as an adhesive agent or circular bandages may be used to keep the dressing in place. If the skin is painted with compound tincture of benzoin before adhesive tape is applied, skin irritation will be less. Small children and infants are more comfortable on firm mattresses than on soft ones; fluffy pillows and bedding afford no support to the baby's body, which rapidly becomes tired in a strained position. Also, while a sick baby should be handled as little as possible, he should be given the benefit of frequent changes in position.

Infants do not tolerate distention well and this common postoperative complication must be combated early by means of stupes, appropriate enemas, and the frequent insertion of a small rectal tube. Feeding in such cases may be done by gavage, if necessary. Sedation after operation is not often needed in infants or very young children; when such medication is required, paregoric, 0.5 to 4 c.c. (dr. 1/8 to 1), according to the age and weight

of the patient, will usually prove satisfactory. For older children a wider choice of sedatives is available (p. 119).

**Aged.**—With the increasing modern life expectancy more old people are requiring surgical treatment every year, and with the improvement in surgical technique and general care better results are being obtained from operation. While it is true that the aged present an increased risk because of the residual effect of previous systemic or visceral disease, much can be done by proper management to render these patients more eligible surgically. Furthermore, the effects of age upon the general health of an individual differ widely in each case; many people of advanced years, in the absence of systemic disease, enjoy excellent health and exhibit marked recuperative powers following operation or illness. Other less fortunate persons much younger in actual years may exhibit a decreased physical reserve as a result of some constitutional or chronic organic disorder. The number of years a prospective surgical patient has lived is of much less importance than the effects the passing years have had upon his mental attitude and general physical condition.

Many individuals, even in middle life, accept the burden that a surgically curable condition imposes rather than submit to operation, solely because of their chronologic age. Recent reports from many large medical centers<sup>3,4</sup> indicate that serious operations may be performed with perfect safety upon the aged patient if proper care is taken to avoid undue strain upon damaged organs and to foresee and prevent the development and progress of postoperative complications. For many years urologic surgeons have been securing excellent operative results in aged patients. As a result of the dread of surgical procedures common among older people, disease processes are very often allowed to progress farther in them than in younger patients before a surgeon is called. Operative mortality and morbidity are increased still further as a result of this tendency, and an excellent surgical risk may be transformed into a very poor one simply by the factor of delay.

**PHYSICAL EXAMINATION.**—The elderly patient should receive an especially thorough examination of the lungs, cardiovascular system, and urinary tract, with laboratory investigation of the blood and urine and of the kidney function. Attention

must be paid not only to the present illness, but also to the effects of associated disease upon the functional capacity and physiologic reserves of the diseased organs.

If generalized arteriosclerosis or cardiac disease is noted on examination or suspected from information secured in the history (Chapter 10), the exercise tolerance of the patient should be determined and an electrocardiogram secured. Investigation of the urinary tract in these patients should include not only a routine urinalysis, phenolsulfonphthalein excretion test, and blood nonprotein nitrogen determination, but also an estimation of the excretory reserve of the kidneys by means of a Fishberg or Mosenthal concentration test. History of a recent or chronic cough or evidence on physical examination of pulmonary changes necessitates an x-ray examination of the chest. When bronchiectasis is suspected, a lateral x-ray should be taken (left side down) as well as an anteroposterior, since early or hilar changes in the left lung may be obscured by the heart shadow.

**PREOPERATIVE PREPARATION.**—Several days may be spent profitably before operation to relieve the dehydration generally present in old people, to augment the glycogen reserve and consequently the hepatic function, and to insure a positive nitrogen balance. A high carbohydrate, high protein, low fat, high vitamin diet is prescribed, with particular emphasis on the patient's food preferences. It is better not to order too heavy a diet; patients with light appetites will eat less if a full tray is presented than if the quantity of food is adjusted to their capacities. Intermediate nourishments are ordered and are made up so that each contains an ounce or more of skim milk powder, whole casein, lactalbumin, or protein hydrolysate, preferably without added fatty foods. More success is attained with the whole proteins mentioned than with protein hydrolysates, as a rule, because of the unappetizing flavor of the hydrolysate preparations. Enough supplementary protein nourishment is supplied to furnish at least 1.0 Gm. per kilogram of body weight in addition to the dietary protein and preferably even more. The presence of actual or borderline hypoproteinemia demands definite planned treatment to correct the deficiency before operation is undertaken.

Anemia, even of slight degree, is far more dangerous in aged surgical patients than in younger ones. One or two trans-

fusions of whole blood, sufficient to bring the red cell count to a normal level, will improve the patient's general condition greatly. Vitamin deficiencies, almost routinely found in older people, can be corrected with ease by the administration of therapeutic amounts of vitamin preparations, particularly thiamine chloride, nicotinic acid, and ascorbic acid. The routine preoperative administration of digitalis has been advocated, but opinion generally is that such a practice is unwise, digitalis being better reserved for patients in whom its use is definitely indicated.

The chief danger attending surgery in the aged lies rather in the complications that develop after operation than in the operation itself. Since the prevention of such complications is less difficult than their treatment, careful nursing is as important as careful surgery. The tendency of aged patients to develop surgical shock is well known; appropriate supportive measures therefore must be instituted in the operating room if the slightest indication for their use arises. When the patient is returned to his room, the pulse, respiratory rate and depth, blood pressure, and general appearance must be watched with the greatest care not only during the immediate postanesthetic period but also during the first forty-eight hours after operation, until the danger of shock or renal failure has passed. Infusions of physiologic fluids, administered slowly, and transfusions of whole blood are to be given without delay if shock is threatened.

**POSTOPERATIVE CARE.**—After operation the patient is returned to a warmed bed and wet clothes are changed at once. If hot-water bottles are used, they should never be allowed to touch the patient, in order to avoid burns. Although proper ventilation of the room must be secured and wet clothes should be changed at once, the aged patient cannot stand exposure to cold air or to drafts.

Measures should be taken to prevent the development of postoperative pulmonary complications, which are so frequent and so often fatal in old people. Some surgeons attempt to forestall pneumonia following severe operations by placing the patient in an oxygen tent at once, even before the need becomes evident. Others, however, believe that pulmonary atelectasis may be encouraged in certain individuals with excessive bronchial secretion by the early postoperative administration of oxygen and consequent diminution of respiratory amplitude<sup>5</sup>



and prefer the use of carbon dioxide inhalations to induce deep respirations and full pulmonary expansion. Hypostatic congestion and atelectasis may also be successfully avoided by frequent changes of position during the first few days, encouragement of active exercising movements of the arms and legs, regular and frequent breathing exercises (for example, the patient may be asked to take a dozen full deep breaths every hour when awake), avoidance of tight dressings, and allowing the patient out of bed as soon as his operative wound and general condition will permit. These precautions cannot be emphasized too strongly, for postoperative pneumonia is one of the commonest causes of death in aged surgical patients. Advocates of early postoperative ambulation stress the facts that pulmonary ventilation is increased and vital capacity is rapidly restored to normal in patients who begin walking a day or two after operation, which make it a procedure particularly valuable in older patients. As a matter of fact, early rising after operation is probably even more advantageous in the aged than in the younger groups.

In order to keep the frequently querulous patient comfortable and contented, sedatives are used as indicated. Codeine, 16 to 45 mg. (gr.  $1/4$  to  $3/4$ ), is usually preferable to morphine, 8 to 10 mg. (gr.  $1/8$  to  $1/6$ ), because of the markedly depressing effect that morphine exerts on the aged individual, both upon the patient as a whole and upon the respiratory center in particular. For the same reason, hypnotics, when used, should be given in smaller than average doses at first. Administration of vitamin B<sub>1</sub> in the usual doses has been suggested as a remedy for sleeplessness in the aged, who often suffer from a subclinical deficiency of this substance.

Proper fluid balance must be maintained, but it may be difficult to persuade the aged individual to take sufficient water by mouth. If evidence of dehydration appears, or if the urinary output decreases too sharply, fluid is administered slowly by vein. When kidney function is poor and fluid is retained, a small quantity (100 to 200 c.c.) of 20 per cent dextrose may be given intravenously.

Postoperative diet should be light and easily digested, high in carbohydrate content and relatively high in protein but correspondingly low in fats, which are more difficult to digest. Just as

during the preoperative period, intermediate nourishments of protein or protein hydrolysate preparations are of the greatest value. In case of necessity, protein hydrolysate solutions may be given slowly intravenously in sufficient quantity to furnish up to 100 Gm. of protein daily, either in place of oral protein supplements or in addition to them. Any special dietary preferences of the patient should be humored as far as possible, and a small amount of whiskey once or twice a day before meals may be a source of great comfort and relaxation to an older person. Confidence and an optimistic attitude are to be fostered, and words of cheerfulness and encouragement from the attending surgeon and nurses are much to be desired. Older patients are likely to become lonely and appreciate short frequent visits more than any other type of patient. Occasionally, sympathetic encouragement and understanding are actually lifesaving; a patient of advanced age who feels sure that he is too old to recover from a major operation will need constant reassurance as much as he needs medical care.

Catheterization of the urinary bladder is avoided whenever possible, for this procedure often initiates a serious infection of the urinary tract in the aged, whose resistance to bacterial infection is low. The various means of inducing spontaneous voiding are usually successful (p. 331), and the patient should be allowed to stand or to use a commode by the bedside during the early postoperative period if necessary, even though the surgeon may not ordinarily favor early postoperative rising. If the patient cannot void and there are definite contraindications to his rising, catheterization may be performed and one ounce of silver nitrate solution (1:1,000) left in the bladder before the catheter is withdrawn. It is worth noting that postoperative distention of the urinary bladder may develop in older patients with almost no symptoms. It is the responsibility of the surgeon and the hospital staff to watch the patient's urinary output until normal bladder function returns.

Finally, the lowered resistance of the skin to trauma must be considered. Old people who are forced to remain in bed for long periods should be allowed to rest upon a rubber ring or an air mattress so that constant pressure upon the sacrum may be avoided. Decubitus ulcers may occur also over the trochanters and in the region of the heels.

### Coincidental Infection

**Oral Sepsis.**—Pyorrhea, stomatitis, and Vincent's angina are often found in the course of the routine physical examination. Such oral lesions have a definite bearing upon the occurrence of postoperative pulmonary complications and efforts therefore should be made to combat mouth infections before operation is undertaken. The causative agent is usually a nonhemolytic anaerobic or microaerophilic streptococcus in symbiosis with the spirillae, spirochetes, and fusiform bacilli commonly found in diseased mouths.

Good therapeutic results are obtained by the local use of oxidizing agents. If the lesions are superficial and mild, sodium perborate (4 per cent solution) may be given as a mouthwash every hour. Hydrogen peroxide (half strength) may be employed as a rinse between applications of sodium perborate. Lesions that are more deep seated, especially about the teeth, sometimes respond more rapidly to the application of sodium perborate as a paste, rubbed into the infected areas every two hours with a gloved finger. The salt is strongly alkaline and is consequently irritating, its use in this way should be restricted to alternate days. Hydrogen peroxide (half strength) may be used hourly in the intervening periods.

Extensive oral or pharyngeal lesions, especially those accompanied by evidences of local inflammation, may prove resistant to the action of ordinary oxidizing agents. In such cases prompt improvement may follow the use of a suspension of zinc peroxide. This preparation, when properly made (p. 486), liberates oxygen at a regular rate for many hours and consequently is highly effective in the treatment of infections caused by anaerobic organisms. Meleney<sup>6</sup> has suggested the use of zinc peroxide as a mouthwash (1 part of powder to 4 parts of water). One mouthful is taken every three to four hours and is thoroughly rinsed around the mouth and between the teeth. No water is taken after the medication is expectorated, so that its action is maintained as long as possible. Lesions in the pharynx or in the tonsillar fossae should be treated with a cotton applicator dipped in the zinc peroxide suspension.

Sulfonamides used locally in treatment of oral infections are of little value. Penicillin may be tried as a local application,

but its effects are inconstant when used in this way. A solution of penicillin in normal salt solution, 250 to 500 units per cubic centimeter, may be supplied as a mouthwash every two to three hours, the solution to be rinsed between the teeth and held in the mouth for a few minutes. Penicillin troches each containing 5,000 units of the drug may be used, although these too are not consistently effective. One troche is dissolved in the mouth every two hours, the resulting solution being retained for several minutes before swallowing. While mild superficial infections may be helped somewhat by local applications, penicillin or sulfadiazine or both in full dosage as for a systemic infection will be much more effective.

**Other Foci of Infection.**—Thorough search must be made if there are indications of the presence of any other focus of acute or chronic infection. Ears, sinuses, teeth, tonsils, lungs, and genitourinary tract may act as sites of latent chronic infection which, if present, may require therapeutic attack before operation. Surgery in the presence of chronic long-standing pulmonary disease, such as tuberculosis, bronchitis, or bronchiectasis, requires division of responsibility for management of the patient with an internist.

**Early Syphilis.**—Early syphilis, untreated and infectious, should contraindicate any elective operation until proper therapy has rendered the individual less dangerous to those who must come into contact with him. Late syphilis, in the absence of changes in the central nervous system, offers little increase in operative risk, in general, unless cardiovascular changes due to the disease are present (Chapter 10).

### Obesity

Obesity in a surgical patient not only adds to the technical difficulties of operation, but also foreshadows certain complications of the postoperative period. Since individuals who are markedly overweight seem to be especially subject to the development of metabolic disease, preoperative examination of the obese surgical patient should include a careful search for evidence of diabetes mellitus, hypothyroidism, cardiac disturbances, arterial hypertension, arteriosclerosis, nephritis, biliary tract disease,

and affections of the respiratory system. If the operation can be postponed with safety, the patient's general condition and surgical acceptability can be improved by administration of a diet adequate in proteins, vitamins, and necessary minerals but low in caloric value, calculated to reduce his weight. Such precautions are of especial value in patients who require hernioplasty.

Preoperative sedation and basal anesthesia are employed to a minimum degree; if such medication is used, the dose should be calculated on the basis of the patient's ideal weight rather than on his actual weight. The immediate postoperative nursing care of an unconscious obese patient is often very difficult, and preoperative medication that produces a prolonged postoperative sleep should be avoided. It is of the greatest importance that a trained attendant, either the anesthetist or a nurse, remain with such a patient until recovery from anesthesia is complete. Respiratory obstruction is likely to take place in these individuals unless the head is extended and the chin held forward; cyanosis and complete cessation of breathing may occur in a very short time in obese anesthetized patients who are left unattended.

Postoperative complications frequent in excessively overweight individuals include vomiting and starvation acidosis, pulmonary atelectasis, bronchopneumonia, intestinal distention, wound infections, venous thrombosis, and skin irritations. Specific preventive measures must be taken and complications must be noted and corrected in their earliest stages. Maintenance of proper fluid intake, frequent change of position, and insistence upon deep breathing and muscular exercises are among the most important prophylactic measures to be followed after operation. Among the minor annoyances that appear during convalescence is pustular dermatitis, usually about the shoulders and back and upon the buttocks. Irritation of the skin in these regions may be prevented by requesting the attending nurse to rub the areas frequently with 50 per cent alcohol to toughen them, to dry the skin carefully, and then to apply talcum powder. Wound infections and liquefactions of subcutaneous fat are also very common in obese patients; such collections of fluid should be evacuated in the proper manner as soon as they develop.

### Malnutrition

Malnutrition is a state of chronic debility caused by imperfect nutrition or improper assimilation of the necessary elements of a well-balanced diet. This type of physiologic disturbance is widespread in occurrence, dietary deficiencies being common for many reasons, such as economic necessity, the desire to maintain a slender figure, or the presence of chronic infection, diseases of the gastrointestinal tract, disorders of the biliary system, malignant disease, and alcohol or drug addiction. The nutritional problems which may accompany surgical disorders require identification and correction before operation can be performed with safety.

When the dietary protein intake is insufficient over a long period, breakdown of body protein will occur, with weight loss and general malnutrition. More advanced stages of protein starvation, as in disease of the gastrointestinal tract, will bring about a diminution in plasma proteins as well. The hypoproteinemia is latent at first, since loss of fluid from the blood plasma will occur concomitantly with the decrease in plasma protein concentration. If infusions of normal salt and dextrose solutions are given in the presence of such a physiologic disturbance, however, plasma dilution and tissue edema may appear as a result of fluid retention. Determination of the plasma protein concentration is indicated as a routine if deficiency is suspected. When the value drops to 5 Gm. per 100 c.c., latent or clinical edema may be anticipated.

Hypoproteinemia, if uncorrected, may interfere seriously with normal wound healing after operation; this deficiency state is often a definite factor in the development of wound dehiscence, weakened tissue repair, and occurrence of infection. Restoration of depleted body and plasma proteins is of the first importance in preoperative care. Even in surgical conditions requiring emergency operation, blood or plasma transfusions are of much value, and subsequent protein replacement therapy may be carried out during convalescence. When operation can be postponed for several days, treatment of malnutrition and hypoproteinemia will more than justify the delay by decreasing the operative risk, decreasing the likelihood of postoperative complications, and shortening the period of convalescence to normal

health. Measures for restoring depleted protein reserves (p. 69) include the prescription of a high protein diet, the administration of extra protein foods (skim milk powder, casein, lactalbumin) or of protein hydrolysates in intermediate nourishments or by stomach tube, the administration of protein hydrolysates by infusion, and the administration of vitamin preparations as indicated.

A great deal of clinical work has been done on the dietary treatment of hypoproteinemia in surgical patients. One of the most important steps was the demonstration by Ravdin and associates<sup>7</sup> of the value of a high carbohydrate, high protein diet containing 20 to 30 per cent protein, 5 to 10 per cent fat, and 70 to 80 per cent carbohydrate, with added vitamin B preparations. By administration through a duodenal feeding tube of a specially prepared peptone hydrolysate with added glucose, sodium chloride, and water, these investigators were able to supply from 65 to 90 Gm. of protein and 200 to 500 Gm. of glucose daily to patients unable to take a proper diet by mouth, as following gastric operations. The combined research of many clinical and laboratory workers, however, has resulted more recently in the development of methods of protein feeding that permit maintenance or even gain of weight in a patient whose gastrointestinal tract is completely at rest. The work in protein nutrition, with the development of pure simple proteins and protein hydrolysates for administration by mouth or by tube and, more especially, the development of protein hydrolysates suitable for intravenous use, has produced one of the most important advances in surgical physiology in recent years. The significance of protein feeding in the care of surgical patients has been discussed in a monograph by Elman,<sup>8</sup> who has done much work in this field.

Chronic malnutrition or metabolic disease may also cause depletion of the body glycogen reserves. Decrease of the liver glycogen, which is necessary for proper functioning of the liver cells and for their protection against the effects of injurious agents, may be followed by fatty infiltration of the liver. Impairment of liver function results and the liver may then be damaged readily by noxious influences to which it is ordinarily resistant. Restoration of the carbohydrate reserve before operation is effected best by administration of dextrose orally or intra-

venously. Displacement of the liver fat deposits by carbohydrate can be accomplished more readily if the dietary protein is increased (p. 56). The type of diet best suited to the correction of hypoproteinemia therefore is well suited also to the restoration of diminished liver glycogen and the improvement of liver function.

### Vitamin Deficiency States

Since the identification and isolation of some of the vitamins necessary for proper nutrition, growth, and maintenance of normal health, much useful and interesting information concerning the specific effects of these substances has been discovered. Each vitamin is required in definite minimal amounts. None can replace any other and none can be stored for any appreciable period. A deficiency of any one vitamin will produce characteristic physiologic effects that can be corrected by administration of the lacking substance in proper amounts.

Vitamin deficiencies are almost always multiple; even though the clinical picture is characteristic of one particular deficiency state, subclinical deficiencies of the others usually also are present. Moreover, vitamin deficiency states that are not clinically apparent before serious illness or operation may become evident during the course of the disease or convalescence. For these reasons, it is best to supply therapeutic doses of all the vitamins that may be lacking when deficiency of a single one is apparent or suspected and to continue treatment over a period of weeks rather than simply for a few days.

Vitamin A, a fat-soluble unsaturated alcohol, has been isolated in pure form; its precursor (carotene) is found especially in liver, milk and milk products, green vegetables, carrots, and fish-liver oil. The vitamin, or rather the provitamin, is absorbed from the intestinal tract in combination with bile acids; fat and bile in the intestine are both necessary for its proper absorption and it is activated and stored in the liver as a fatty acid ester. This vitamin is necessary for proper functioning of the epithelial surfaces throughout the body, including those lining the alimentary, respiratory, and urinary tracts. Deficiency of the substance results in keratinization of the epithelium in these systems, with an increase in susceptibility to infections of the epithelium-lined tracts (especially the respiratory system). Skin



lesions, boils, and often affections of the eyes are noted to result from vitamin A deficiency. Therapeutic use of the pure vitamin is indicated not only to correct obvious deficiency states, but also to increase the bodily resistance to infections when the vitamin A intake has been subminimal over a long period. A deficiency of this substance always occurs in conjunction with diseases in which the bile necessary for absorption of the fat-soluble vitamin has been prevented from entering the intestinal tract, as in obstructive jaundice. The average daily requirement is considered to be from 4,000 to 5,000 units. Vitamin A may be supplied in severe cases of deficiency in doses of 50,000 units daily and in mild cases by increasing in the diet the quantity of foods containing this substance. Overdoses apparently produce no deleterious effects.

Vitamin B complex has been separated into many different components, including thiamine, nicotinic acid, riboflavin, pyridoxine, pantothenic acid, choline, inositol, para-aminobenzoic acid, biotin, and folic acid (p. 218). Of these factors, the first three are of particular importance, especially in the care of the surgical patient. The combination of all these substances is of primary necessity in the bodily economy, growth, and metabolism of the living organism. Several of them and probably all of them function as active participants in the enzyme systems mediating cellular respiration and oxidation-reduction reactions.

Clinical deficiency of single components of the vitamin B complex, while existing as well-defined disease entities, always indicate less severe associated deficiencies of other components of the complex. In treatment, one fraction should not be administered alone; proper therapy requires administration of full doses of all the B factors, or at least of the three best-known ones (thiamine, nicotinic acid, and riboflavin), in proportionate dosage. Use of these vitamins probably is of particular value in patients receiving repeated doses of dextrose intravenously, since the vitamin B complex requirement is increased by a high carbohydrate intake.

*Thiamine hydrochloride* (vitamin B<sub>1</sub>) is water soluble and has been isolated and synthesized. This substance is widely distributed in nature and is found in large quantities in fresh fruits and in the hulls of grains (rice polishings, wheat germ, whole-grain

cereals); it also occurs in leguminous vegetables, milk, and nuts and in some viscera (liver, kidneys). Vitamin B<sub>1</sub> is necessary in the intermediary metabolism of carbohydrates, probably serving as an active coenzyme, and is also required for normal functioning of nerve tissues and for normal growth and development of the entire body. Deficiencies of the substance may produce such effects as anorexia with loss of weight, weakness of the quadriceps muscles, hypoactivity of the tendon reflexes in the legs, hyperesthesia of the feet and calves, improper carbohydrate metabolism with accumulation of intermediary products (lactic acid, pyruvic acid) that may damage the nervous tissues, impaired functioning of the gastrointestinal tract or of the cardiovascular system on a nutritional basis, delayed wound healing, and multiple neuritis (beriberi) with generalized edema, serous effusions, and muscular atrophy. Therapeutic administration of the pure substance is indicated in the preoperative treatment of any surgical disease that has been accompanied by anorexia, loss of weight, restricted diet, increased metabolic rate, long-standing fever, or continued vomiting, as well as in the treatment of hypoproteinemic states, nutritional edema, and chronic alcoholism. The requirement of thiamine in normal health averages about 0.6 mg. for each 1,000 calories of the diet, a daily total of from 1.5 to 2.0 milligrams. Somewhat larger quantities are required with high carbohydrate diets.

Deficiencies of this substance in adults respond well to doses of 10.0 to 20.0 mg. of thiamine hydrochloride administered either orally or parenterally once or twice a day. Overdoses of thiamine apparently produce no ill effects except in occasional instances when large doses of the vitamin are given without the simultaneous administration of other members of the vitamin B complex. Brewers' yeast tablets, in doses of three to eight tablets three times a day, serve as a valuable and less expensive source of vitamin B<sub>1</sub> for oral use.

*Nicotinic acid* (niacin), the pellagra-preventive factor, is water soluble and has also been isolated and synthesized. This substance occurs in rice polishings, wheat germ, liver, kidney, and yeast. Smaller amounts are found in buttermilk, green peas, and tomato juice. Although closely related structurally to nicotine, the vitamin exhibits none of the toxic physiologic effects of nicotine upon the body. Nicotinic acid, like thiamine, takes

part in the intermediary metabolism of carbohydrates, the daily requirement for the vitamin consequently rising with increase in the dietary carbohydrate. The average daily requirement of nicotinic acid is from 10 to 20 mg. daily in health.

Deficiency of this vitamin is responsible for the development of pellagra. Because this disease is relatively common in certain geographic areas and because the early manifestations may appear in such varied clinical forms, the possibility of subclinical pellagra or at least of a nicotinic acid deficiency must be considered in evaluating the condition of any patient whose diet has been restricted. For subclinical deficiencies and for prophylactic use in general malnutrition, nicotinic acid is given in doses of from 100 to 200 mg. in divided doses daily. Nicotinic acid occasionally induces flushing of the skin and itching; nicotinic acid amide (niacinamide) is fully as effective as niacin and does not exhibit these slight toxic effects. It may be stated parenthetically that Goldzieler and Popkin<sup>9</sup> have found the slow intravenous administration of 100 mg. of sodium nicotinate to be effective in relieving severe headaches, even migraine.

*Riboflavin*, or vitamin G, a water-soluble yellowish pigment, has also been isolated and synthesized. This substance occurs in the natural state in milk, eggs, kale, spinach, wheat germ, and liver. Riboflavin is also concerned in the oxidation processes of the cell as an enzyme and may be a factor in the normal growth and development of the body. Deficiency of riboflavin is manifested by weakness, insomnia, and anorexia and more characteristically by cracks and macerated areas at the angles of the mouth (cheilosis) as well as by chronic conjunctivitis and impairment of vision. The requirement of riboflavin in health is from 2 to 3 mg. daily. Use of this vitamin is indicated in conjunction with administration of other members of the vitamin B complex, as well as in specific treatment of ariboflavinosis, the dose varying from 3 to 5 mg. three times daily, according to the indication.

*Pyridoxine* (Vitamin B<sub>6</sub>) is water soluble and occurs particularly in meat, wheat germ, and vegetable fats. While the specific functions of this substance have not been established, it has been claimed to be of some value as an adjunct in the treatment of agranulocytosis, as, for example, that due to thiouracil toxicity, and in "radiation sickness." No daily requirement has been

established, of course; therapeutic doses employed have varied from 25 to 100 mg. a day.

The therapeutic value of other components of the vitamin B complex, such as pantothenic acid, biotin, inositol, choline, and para-aminobenzoic acid, have not been well enough established as yet to warrant their use.

Vitamin C (ascorbic or cevitic acid) is a relatively simple water-soluble substance that has been isolated and synthesized. This vitamin occurs in large quantities in citrus fruits, tomatoes, and raw cabbage. It is necessary for the normal development and maintenance of collagen and of the intercellular cement substance both in normal health and in the healing of wounds and fractures. The suggestion has also been made that vitamin C is closely associated with specific antibody synthesis and with occurrence of allergic and anaphylactic manifestations.

Advanced deficiencies of this substance result in scurvy or scorbutic changes such as localized hemorrhages due to general weakening of the capillary walls, bleeding gums, pyorrhea, and painful joints. Subclinical deficiencies in surgical patients result in delayed and weakened healing of wounds and fractured bones and in decreased resistance to infection. Fairly satisfactory laboratory tests upon blood plasma and urine for the determination of avitaminosis C have been devised. Therapeutic administration of this vitamin is indicated in the deficiency states described, as well as in suspected avitaminosis as a result of restricted diet, febrile states, gastrointestinal disease, or some similar debilitating influence. Delay in healing of a wound should always demand consideration of avitaminosis C. Deficiency is often noted in patients with peptic ulcer or any condition in which hematemesis is found and operation in such cases should be preceded by vitamin C therapy. For therapeutic use ascorbic acid is given orally or parenterally in doses of 300 to 500 mg. one or two times a day. Since the average daily requirement is relatively high (30 to 40 mg.), deficiency of this vitamin is very common.

Vitamin D, which is fat soluble, is produced in pure form (calciferol) by irradiation of ergosterol with ultraviolet light. Another form of vitamin D, closely related to calciferol in chemical structure and somewhat more potent clinically, is found in hali-

but-liver oil and is also produced in the skin following ultra-violet irradiation.

While vitamin D is, of course, specific in the treatment of rickets, its therapeutic use in surgical patients is indicated chiefly in conditions associated with abnormalities of calcium and phosphorus metabolism due to deficiency of the vitamin. Since its presence is necessary for normal bone growth, it is sometimes used as an adjunct in the treatment of fractures. Under these circumstances an adequate supply of calcium and phosphorus also must be provided. Overdosage of the vitamin does not produce harmful results in adults if it is not administered over too long a period and if the mineral intake is sufficient. The dosage varies with the type of preparation used; probably 1,000 to 2,000 U.S.P. units daily will prove ample to assure proper formation of callus in fractures of bone. The average daily requirement in health is from 400 to 800 U.S.P. units.

Vitamin E, which is fat soluble, has been isolated and synthesized. This substance, the antisterility vitamin, is chiefly concerned with the normal process of reproduction, as far as is known at present, and is consequently of little primary interest to the surgeon. It has been used without much success in treatment of muscular dystrophies. More recently, the use of vitamin E (alpha-tocopherol) has been advocated in the treatment of early peripheral vascular disease (p. 767).

Vitamin K, which is fat soluble, has been isolated in different forms; that is, several substances with high vitamin K activity have been synthesized, the simplest and most effective being 2-methyl-1,4-naphthoquinone. This vitamin is found in green leafy vegetables, as well as in soybean oil and egg yolk.

It is necessary for the synthesis of prothrombin by the liver and its absence from the diet is responsible for a decrease in blood prothrombin and consequently for a hemorrhagic tendency. Since the vitamin is fat soluble, bile is required for its absorption from the intestine. Clinical deficiency states of vitamin K, marked by a prolonged coagulation time of the blood, are found therefore in association with obstructive jaundice as well as with pyloric obstruction and severe diarrhea. Evidence of the deficiency may be found by determination of the prothrombin level in the blood. Vitamin K has also been used with success in treating

hemorrhagic disease of the new born when the bleeding tendency is due to blood prothrombin deficiency. Therapeutic use of vitamin K in the form of synthetic menadione or of an allied compound is indicated particularly in treatment of the bleeding tendency accompanying obstructive jaundice. It is administered orally in doses of 1 to 2 mg. together with bile salts, 0.3 to 0.6 Gm. (gr. 5 to 10), three times daily, or parenterally in similar dosage without bile salts (p. 706).

### Anemia

Many conditions may be responsible for the occurrence of chronic anemia in surgical patients. Whatever the initiating cause may be, the deficiency in hemoglobin must be discovered and corrected before operation.

Decrease in the normal hemoglobin level may be brought about in three ways: by blood loss, either acute or chronic, by intravascular destruction of erythrocytes, as in hemolysis, or by deficient production of erythrocytes. The etiologic factor responsible for the development of the anemia must be identified so that proper treatment can be instituted for the specific type present.

In recent years there has been a growing tendency to abandon the classification of anemias as primary and secondary, since all depressions of hemoglobin and of red blood cells necessarily must be due to some causative factor or factors and therefore must be secondary. Anemias are currently classified<sup>19</sup> either in descriptive terms, such as normocytic, microcytic, or macrocytic, and hypochromic or hyperchromic, or in terms of the causative factors, such as anemias due to excessive blood loss (hemorrhagic or hemolytic), anemias due to a deficiency, and anemias due to disturbances of the bone marrow. Anemia due to blood loss is the type most commonly encountered in surgical patients.

Acute hemorrhage, with the loss of a relatively large quantity of blood during a short period of time, presents the picture of a surgical emergency. The symptoms and treatment of the condition depend largely upon the location, extent, and initiating cause of the hemorrhage. Rapid loss of a large amount of blood always produces certain typical systemic symptoms, no matter what the lesion responsible for the hemorrhage may be

(p. 350). Proper therapy includes prompt control of the bleeding vessel and replacement of the lost blood by transfusion

**Chronic secondary anemia**, or chronic hypochromic anemia due to blood loss, is commonly the result of continued intermittent hemorrhage in surgical patients who present an ulcerating lesion such as peptic ulcer, carcinoma of the gastrointestinal tract, or bleeding hemorrhoids. In any such condition constant loss of small amounts of blood over a long period of time will often result in the development of a severe anemia; the patient's hemoglobin may be depressed to 25 per cent simply by slight and unnoticed hemorrhage from an ulcerating hemorrhoid. Usually associated are chronic dehydration, malnutrition, and hypoproteinemia, with all the added problems that these states present. Anemic patients characteristically exhibit general weakness, anorexia, and pallor, and examination of the blood reveals a low red cell count, decreased hemoglobin, and typical abnormalities in the appearance of the erythrocytes. The red blood cells in anemia secondary to chronic blood loss are microcytic and hypochromic, the color and volume indices are low and the mean corpuscular hemoglobin concentration is subnormal.

Certain systemic factors may aggravate anemia due to blood loss. Malignant tumors often appear to exert a retarding influence upon hematopoiesis, so that anemia may develop far in excess of that which might be explained by hemorrhage alone. Sepsis, particularly the type due to pyogenic infections or chronic respiratory tract disease, may also depress the activity of the bone marrow. The degree of anemia that results from the effects of bacterial toxins depends largely upon the type, location, duration, and extent of the infection and upon the state of resistance and general nutrition of the patient.

Various parasitic infections often produce a similar type of anemia, with toxic depression of hematopoiesis as well as actual blood loss; sometimes, as in malarial infections, hemolysis may occur within the blood stream. *Infection with intestinal parasites* is especially common in warmer climates and frequently causes advanced degrees of anemia.

The hypochromic microcytic anemia that is sometimes found in middle-aged women, often associated with achlorhydria, is similar to other forms of chronic iron-deficiency anemia with

respect to symptoms and blood changes. The disease probably is due to chronic blood loss from menorrhagia with deficient regeneration, and the accompanying achlorhydria apparently interferes with proper absorption of iron from the diet. Menorrhagia, however, may produce a marked hypochromic anemia in any adult female patient.

Preoperative correction of an anemic state should cover as long a period of time as possible to enable the patient to regain strength and to repair the systemic damages caused by chronic illness. The usual measures indicated for treatment of malnutrition as well as those indicated for treatment of the anemia are employed. No major operation, except in case of emergency, should be undertaken on any patient whose hemoglobin is below 80 per cent (11.7 Gm.) or whose red blood cell count is below 4,500,000 per cubic millimeter. Such patients are highly susceptible to operative shock, for the circulatory reserve is decreased and the oxygen carrying capacity of the blood is limited. Enough time should be taken before operation to restore the fluid deficiency and to correct the anemia, either by transfusion of whole blood or by administration of iron compounds as indicated. Preoperative preparation of anemic patients must not be too hasty; the effects of a chronic and debilitating illness cannot be corrected by a few days of intensive treatment.

**TREATMENT OF CHRONIC SECONDARY (IRON-DEFICIENCY) ANEMIA.**—Patients with anemia secondary to chronic blood loss or to a diet deficient in iron content will respond strikingly to the therapeutic administration of iron compounds. If the source of chronic blood loss is controlled or removed, inorganic iron will produce effects in this type of anemia almost as specific as those produced by liver extract in pernicious anemia.

Iron preparations are given in large doses. The amount administered must be far in excess of that theoretically required, since only a fraction of the iron absorbed is utilized in the formation of hemoglobin and since there is great individual variation in response to small doses of iron. Because of the large amount required, the medication is administered in divided doses during the day. These drugs are tolerated best after meals, when the danger of gastric irritation and nausea is minimized.



Various preparations are available. In general, ferrous salts are most effective and smaller doses of iron in this form may be used. Ferrous sulfate, probably the most efficient preparation, is given as enteric-coated tablets in doses of 0.2 Gm. (gr. 3) four times daily or as an elixir in similar dosage. Ferrous carbonate (Blaud's pill) is often used, but the therapeutic effectiveness of this medication is lessened by the fact that unusually large doses must be given (at least five 0.3 Gm pills three times daily). Dehydration and desiccation of these tablets is likely to occur; unless ferrous carbonate tablets are freshly made, they may pass through the intestinal tract unchanged. Ferric ammonium citrate may be used in capsules or in solution (25 per cent) and is administered in doses of 2.0 Gm (gr. 30) three times daily. Solutions of iron compounds are best given through a straw or drinking tube to avoid discoloration of the teeth.

There is little to be gained by the administration of proprietary medications containing added copper or vitamins, if these factors are indicated, they may be given separately. Although liver extracts are not specifically indicated in the treatment of secondary (chronic iron-deficiency) anemia,<sup>11</sup> they appear to be of value as a therapeutic adjunct to ferrous iron when the hemoglobin is unusually low. A high protein, high carbohydrate diet is of definite value. Blood transfusions are rarely necessary unless the hemoglobin is below 80 per cent or unless the preoperative period is too short to allow sufficient time for iron therapy.

Anemia associated with sepsis or malignant disease does not show as favorable a response to iron therapy as simple chronic hemorrhagic anemia. Repeated blood transfusions are needed to initiate a hematopoietic response or to support an insufficient one.

Hemolytic jaundice, congenital or acquired, is characterized by the presence of many small spherocytic erythrocytes with increased fragility. The abnormal fragility of the red blood cells is demonstrable clinically as a decreased resistance to hemolysis in hypotonic salt solution. While blood transfusions are often necessary to make a profoundly anemic patient with this disease an acceptable surgical risk, only enough blood should be given before operation to make the surgical procedure possible. Transfusion of blood in these patients is likely to precipitate

further hemolysis, with the result that the patient's condition becomes worse than before the transfusions were administered. There is, of course, no contraindication to the use of blood transfusions as needed after the spleen has been removed.

**Sickle-cell anemia**, which occurs almost exclusively in Negroes, is of common occurrence and is a very real factor in increasing the operative risk. The sickling tendency of the erythrocytes is congenital and familial, but true sickle-cell anemia occurs in only an undetermined percentage of those patients whose erythrocytes exhibit the characteristic change in shape.

The presence of an unexplained anemia in a Negro patient should always demand examination of a blood preparation. In the test for the sickling tendency a drop of fresh blood is diluted, as in the performance of an erythrocyte count, and placed in the center of a cover slip; the glass mount is inverted upon a hollow-ground slide and rimmed with petroleum jelly to prevent evaporation. A positive reaction, with sickling or elongation of most of the erythrocytes, usually will appear within a short time, although the preparation should be allowed to stand at room temperature for twenty-four hours. Occasionally a stained smear of fresh blood will show many sickle forms.

If the routine performance of this test on all Negro patients is not possible before operation, at least all of the individuals who exhibit any of the systemic changes characteristic of the disease must be investigated. Typical associated findings in patients with active sickle-cell anemia include chronic indolent leg ulcers, cardiac hypertrophy without valvular or arterial disease, a history of occasional attacks of abdominal or joint pains, and chronic anemia.

The degree to which the condition affects the operative risk depends entirely upon the stage and the severity of the disease. No special measures of preparation are possible except to combat the anemia by means of blood transfusions. Although sickle-cell anemia is of the hypochromic type, there is little or no response to iron therapy.

**Pernicious anemia**, otherwise called primary anemia or macrocytic hyperchromic anemia, is caused by deficiency of a specific principle which is normally formed in the body by combination of a substance secreted by the gastric mucosa with a

substance found in the diet. This antianemic principle is stored in the liver; liver extract is used as specific therapy. Folic acid, a component of the vitamin B complex, has been shown<sup>12</sup> recently to be also of some value in the treatment of macrocytic anemia. Iron medication is usually given also in pernicious anemia, and whole blood transfusions may be of accessory value if the red cell count is greatly depressed. Pernicious anemia in a surgical patient increases the operative risk and therefore requires the care of an internist as well as a surgeon.

### Hemorrhagic Tendencies

Bleeding tendencies are of three general types, those due to defects in the capillary walls with increased permeability resulting, such as scurvy; those due to defects in the coagulating mechanism of the blood with no alteration in capillary permeability, such as hemophilia and the prothrombin deficiency in obstructive jaundice; and those due to a defect in both the coagulating mechanism and capillary permeability, such as thrombocytopenic purpura.

Scurvy is no longer a common cause of hemorrhage. The characteristic bleeding tendency in the scorbutic adult is manifested by spontaneous hemorrhages about the gums and in the skeletal muscles, with the occasional appearance of petechial hemorrhages in the skin. Diagnosis is made on the basis of the history, examination, and therapeutic test administration of vitamin C. Blood examination reveals no hematologic change except perhaps a chronic posthemorrhagic anemia. In scurvy, the level of ascorbic acid in the blood is always well below the normal value of 0.7 to 1.0 mg. per cent and may even approach zero. Capillary resistance is tested by the application of a sphygmomanometer cuff to an arm and maintenance of a pressure midway between systolic and diastolic arterial pressures for ten minutes. Release of pressure may be followed by petechial hemorrhages; comparison with a normal individual is usually made.

Hemophilia, a hereditary, sex-linked blood dyscrasia, is seen only in the male sex. The increased bleeding tendency is exceedingly dangerous, since such an individual may bleed to

death from a slight injury. There is no constitutional abnormality of any sort except a prolonged coagulation time of the blood. The bleeding time is normal and the clot retracts normally, although several hours are sometimes required for the clot to form. The disease, which is hereditary, is thought to be due to a defect in the blood platelets which are abnormally stable and do not release thromboplastin at the normal rate, with a resultant delay in formation of the clot.

Operation upon such a patient without preoperative recognition of the condition is likely to result in death from uncontrollable postoperative hemorrhage. The routine history in every male patient should include a question concerning the presence of a bleeding tendency, and, if the possibility of hemophilia is indicated even remotely, the blood-clotting mechanism should be investigated with particular attention to coagulation time determination. No specific treatment is possible, but the clotting time may be brought within the normal range for a short time by frequently repeated transfusions of normal blood. Elective operations upon such patients are to be discouraged. Bleeding from accessible areas such as a laceration or a tooth socket can be controlled by application of thrombin (topical) solution with gelatin sponge (p. 490).

Recent work indicates that the coagulation defect in hemophilia is accompanied by, if not actually due to, a defect in some activity of the plasma globulin. A globulin fraction has been isolated<sup>12</sup> which, upon intravenous administration, causes a marked acceleration of coagulation time of several hours' duration in hemophilic subjects. Repeated injections apparently are efficacious. Further work on this subject is being performed.

**Bleeding Tendency in Jaundice.**—Formerly thought to be based upon a deficiency in serum calcium available for clot formation, the hemorrhagic diathesis characteristic of obstructive jaundice is actually due to a deficiency in plasma prothrombin. Prothrombin is normally synthesized in the liver in the presence of an adequate supply of a dietary factor which has been named vitamin K. This substance is found especially in green leaves (spinach, cabbage, alfalfa). Since it is fat soluble, the exclusion of bile from the intestinal tract will prevent normal absorption of the vitamin. Synthesis of prothrombin therefore is prevented

and the normal clotting mechanism of the blood is disturbed. Relief of the hypoprothrombinemia may be accomplished rapidly by oral administration of menadione (2-methyl-1,4 naphthoquinone), a synthetic substance with an activity even greater than that of the natural vitamin K concentrates, or by parenteral administration of one of its soluble derivatives (p. 706).

Since the bleeding tendency is due to a deficiency in prothrombin rather than to the jaundice itself, the same hemorrhagic predisposition will be found following any condition which tends to reduce absorption of fats, and consequently of vitamin K, from the intestinal tract. It may occur as a result of pyloric or intestinal obstruction or of high intestinal fistulas as well as following injury to the liver or the biliary tract. Prolonged coagulation time of the blood, however, is not ordinarily found in association with any form of jaundice except the types associated with extrahepatic biliary tract obstruction or with injury or disease of the liver and consequent hepatic insufficiency. The blood normally contains such an excess of prothrombin that a hemorrhagic tendency based on prothrombin lack does not become clinically apparent until the concentration of this substance has decreased to about 20 per cent of the normal value.

Preoperative tests for the presence of the bleeding tendency due to blood prothrombin deficiency must be performed in every case of the aforementioned pathologic states. Prolongation of the bleeding time, coagulation time, and clot retraction time, although present in case of prothrombin deficiency, are not specifically diagnostic of this condition, for these findings may occur in association with other blood deficiencies.

Several tests for the determination of the hemorrhagic tendency due to hypoprothrombinemia have been described and are to be found in most recent laboratory manuals. The most widely used test is probably the prothrombin time determination according to the method of Quick, which is based upon the physiologic principles involved in blood clotting. Normal blood contains prothrombin and calcium, which react in the presence of thromboplastin (ordinarily derived from blood platelets or tissue fluids) to form thrombin. The activated thrombin reacts with fibrinogen, a plasma protein, to form fibrin strands, which solidify to form a clot. When blood is withdrawn for performance of a test, the immediate addition of oxalate solution immobilizes the blood

calcium and prevents its interaction with prothrombin and thromboplastin. In performance of the test upon oxalated blood, therefore, the specimen is centrifuged to obtain plasma, an amount of thromboplastin fully adequate to insure rapid coagulation is added, and after thorough mixing has been obtained, a standard calcium chloride solution is added in sufficient quantity to permit complete coagulation in the specimen. The number of seconds between addition of calcium solution and earliest appearance of recognizable fibrin formation is designated as the prothrombin time. By reference to a graph (Fig. 15),<sup>14</sup> the prothrombin time can be correlated with the amount of prothrombin in the blood in terms of percentage of normal.

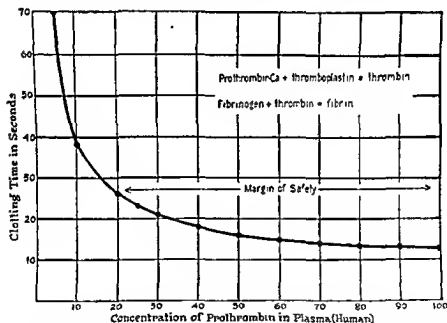


Fig. 15—Quantitative determination of prothrombin, relationship of the clotting time of recalcified plasma (with excess thromboplastin) to the concentration of prothrombin. (Modified from Quick. *Am J Clin. Path* 10: 222, 1910, Williams & Wilkins Co.)

1. The Quick prothrombin time determination<sup>15</sup> is performed as follows:

Nine volumes of blood obtained by venipuncture are mixed with one volume of 0.1 mol sodium oxalate. Usually 4.5 c.c. of blood is a suitable amount, but in the case of the newborn as little as 0.9 c.c. of blood is sufficient. The specimen is centrifuged to obtain a clear plasma.

In a small test tube 0.1 c.c. of the plasma is mixed with 0.1 c.c. of thromboplastin, and recalcified with 0.1 c.c. of 0.025 mol calcium chloride. The time from the addition of the calcium to the formation of the clot is recorded with a stop watch. The test is carried out in a water bath kept at 37.5° C. It is necessary to keep the mixture agitated by frequent gentle tilting of the tube. The clotting time can be directly converted to concentration of prothrombin in per cent of normal by the following equation:

Prothrombin concentration =  $\frac{K}{c.t. - a}$     c.t. = clotting time. K is a constant having the value of 302, and a is a second constant with a value of 8.7.

Thus, if a clotting time of 21 seconds is obtained, the prothrombin concentration is  $\frac{302}{21 - 8.7} = 25$  per cent of normal.

The determination requires an active thromboplastin which must be prepared as follows. The brain of a freshly killed rabbit is freed of all visible blood vessels and macerated in a mortar under acetone. The process is repeated with fresh acetone until the material is granular. The product is dried on a suction filter and then put in small glass vials which are evacuated and sealed. For convenience, 0.3 Gm. is put in a vial. This amount when mixed with 5 c.c. of physiologic saline solution and incubated at 45 to 50° C. for 15 minutes will yield a preparation which will clot normal human plasma under the conditions of the test in 11 to 12 seconds. The saline extract of thromboplastin should not be centrifuged. The supernatant liquid after the coarse particles have been removed by sedimentation is used.

The solution of sodium oxalate is made by dissolving 1.34 Gm. of anhydrous pure sodium oxalate in 100 c.c. of distilled water. The calcium chloride solution is prepared by dissolving 1.11 Gm. of anhydrous chemically pure calcium chloride in 100 c.c. of distilled water.

More recently, Quick<sup>16</sup> has suggested a minor change in the procedure, stating that better results are obtained by the use of 0.02 M. calcium chloride, prepared by dissolving 1.11 Gm. of anhydrous calcium chloride in 500 c.c. of distilled water instead of in 100 cubic centimeters.

The chief defect of the test is that it will not demonstrate the presence of a plasma prothrombin deficiency with accuracy unless the concentration has dropped to 40 per cent of normal or less, when the prothrombin time is prolonged from a normal of 11 to 12½ seconds to an abnormal 15 seconds. This disadvantage may be overcome by repetition of the procedure upon

plasma that has been diluted by the addition of an equal volume of normal salt solution. A prothrombin concentration of, for example, 60 per cent of normal therefore will be reduced to 30 per cent and a prolonged clotting time will be demonstrable.

Performance of prothrombin time determinations on diluted plasma is advocated also by other writers. Allen, Julian, and Dragstedt<sup>17</sup> suggest the use of ten samples of plasma in dilutions ranging from 50 per cent to 5 per cent of the original. Since little prolongation of prothrombin time is noted until the concentration has dropped to a fraction of the normal, it is only by use of serially diluted plasma that lesser depreciations in prothrombin can be detected. Another source of error in interpretation of the results is based on the fact that there is a wide variation of prothrombin between normal limits in plasma from healthy subjects used as controls. Aggeler and co-workers<sup>18</sup> have suggested that blood from at least five normal subjects be tested and the results averaged to obtain a more dependable normal standard. It is therefore strongly advisable always to insure the accuracy of the test by performing it upon several freshly drawn normal control bloods and upon at least one specimen of diluted (50 per cent) plasma as well as upon the undiluted plasma.

2. A simple but only roughly accurate clinical test has been devised by Smith and associates<sup>19</sup>

With a serologic pipet, 0.1 c.c. of thromboplastin, described in the next paragraph, is placed in a small serologic tube (75 by 10 mm. outside diameter). In the tube is then placed blood, freshly drawn from the patient, up to a 1 c.c. mark previously made on the side of the tube. The tube is at once inverted over the finger to obtain complete mixing of the blood and thromboplastin. The tube is tilted every second or two in order to observe clotting. As a control, the test is also carried out on the blood of a normal subject. The calculation is as follows:

Clotting activity (in percentage of normal) =

$$\frac{\text{Clotting time of normal control}}{\text{Clotting time of patient's blood}} \times 100$$

Thus, if the patient's blood clotted in forty-eight seconds and the normal person's blood in twenty-four seconds, the clotting activity is calculated to be 50 per cent of normal.\*

\*It is important to avoid drawing tissue juice into the syringe while making the venipuncture. It is also important that the needle and syringe be entirely free of clots. If there is much difficulty in entering the vein, the sample should be discarded and another sample collected with clean equipment.



To prepare thromboplastin, fresh lung of ox or rabbit is ground, and to each 10 Gm portion is added 10 cc of physiologic solution (0.9 per cent) of sodium chloride. This is stirred at intervals for several hours. The fluid then obtained by straining through gauze is the "thromboplastin" employed in the test described. This thromboplastin keeps well in the ice box.

This procedure is less accurate than the Quick prothrombin time determination and is really more a measure of the clotting activity of the specimen than an actual estimation of prothrombin content. Little prolongation of clotting is noted unless the plasma prothrombin concentration has dropped to less than 40 per cent of normal. In interpretation of this test, any depression of the patient's clotting activity below normal should be considered to signify a probable depression in plasma prothrombin.

Clinical experience has demonstrated that patients who show a plasma prothrombin value of 40 to 70 per cent of that exhibited by normal control subjects are in definite danger of postoperative bleeding, while values below 40 per cent may be assumed to indicate a fully established bleeding tendency. Since the prothrombin content of the blood may decrease by as much as 20 to 25 per cent following operation, an excess of prothrombin well beyond the minimum quantity required for normal clotting (approximately 20 per cent of normal) is required. Consequently when the plasma prothrombin is found to be 70 per cent of the normal or less, specific therapeutic measures are indicated before operation is undertaken (p. 706).

**Purpura hemorrhagica** is of two major types. Thrombocytopenic purpura is associated with a marked deficiency in blood platelets, either on an idiopathic basis or in association with aplastic anemia and a damaged bone marrow. The second type of purpura is based primarily upon capillary damage, either on a probable allergic basis (Schönlein-Henoch) or on a toxic basis (drug poisoning, septic infections). In the latter types, the mechanism of coagulation is normal, the bleeding time is variable, the tourniquet test is usually positive, and the blood platelets are not depressed.

Probably the only form of purpura hemorrhagica that is of particular interest to the surgeon as a factor complicating operation is the idiopathic thrombocytopenic type. Identification of

this disease is not difficult. Bleeding time is prolonged and spontaneous hemorrhage may occur; coagulation time of the withdrawn blood is normal, although the clot does not retract after it has formed. Examination of the blood reveals a marked reduction in blood platelets, the count sometimes dropping well below 50,000 per cubic millimeter. The tourniquet test (p. 218) is usually strongly positive, petechial hemorrhages appearing below the point of application.

The disease exhibits remissions, and spontaneous improvement may occur after an interval. If the patient is being prepared for operation, several transfusions of whole blood will restore the normal clotting mechanism for a short time, but the improvement will continue only as long as the transfused platelets persist in sufficient numbers in the circulating blood.

An interesting preliminary report by Allen and associates<sup>20</sup> suggests the intravenous injection of either protamine sulfate or toluidine blue in combination with whole blood transfusions for prompt temporary control of the bleeding tendency in thrombocytopenic purpura. The theory is advanced that in this type of purpura, an increased amount of heparin-like substance is present in the blood and can be bound and rendered biologically inactive with respect to coagulating activity by means of these drugs. Best results were reported by joint administration of whole blood to restore platelet activity and of toluidine blue or protamine sulfate to help correct the capillary defect and prevent petechial oozing. The authors advise a preliminary test for increased heparin tolerance before use of the compounds. The therapeutic dosage suggested amounts to 2.5 mg. of either toluidine blue or protamine sulfate per kilogram of body weight to be dissolved in 250 c.c. of sterile normal salt solution and slowly administered intravenously over a two-hour period. A dose of 1.5 to 2.0 mg. per kilogram of body weight is given similarly the next day and at intervals as necessary thereafter. Both drugs appear to be nontoxic, although the dye colors the urine and stool. Neither compound is effective orally. Experience with these drugs is too limited as yet to warrant recommendation of their use, but further clinical trial appears to be worth while.

**Summary.**—The various hemorrhagic tendencies can be differentiated by examination of the blood constituents and the clotting mechanism:

1. Scurvy, or avitaminosis C, is characterized by abnormal capillary fragility, which is demonstrable by the tourniquet test, but the constituents of the blood and the coagulation mechanism are normal. Ascorbic acid content of the blood is well below the normal level of 0.7 to 1.0 mg. per cent.

2. Hemophilia is characterized by an abnormality of the blood platelets, which, although normal in number and in appearance, apparently are resistant to destruction. The coagulation time of the blood is prolonged, although the bleeding time is normal, and the clot, once it has formed, retracts normally.

3. Prothrombin deficiency, which is responsible for the bleeding tendency in jaundice due to extrahepatic biliary obstruction or to severe liver damage, results in a disturbance of the entire clotting mechanism as a result of the withdrawal of a necessary constituent. Since prothrombin, activated by thromboplastin, combines with calcium to form thrombin, which will transform fibrinogen into fibrin, its presence in sufficient quantity is required for clotting to occur. Deficiency results in an increased coagulation time and often in a prolonged clot retraction time, the degree of prolongation depending upon the degree of prothrombin deficiency. The other normal constituents of the blood may show no significant alteration.

4. Purpura hemorrhagica of the idiopathic thrombocytopenic type is associated with an increased bleeding time. The clotting time is normal, but the clot does not retract. Examination of the blood reveals a marked deficiency in platelets. The tourniquet test is usually positive.

Scurvy and prothrombin deficiency may be cured readily by specific therapy, but the only treatment possible at present for hemophilia or thrombocytopenic purpura in preparation of the patient for operation is the administration of transfusions of whole blood at frequent intervals.

### Pregnancy

While it is a normal biologic state, pregnancy contraindicates elective intercurrent surgery. If operation must be performed and if it is possible to choose a time, the most favorable period is between the sixteenth week and the sixth month, for during this period abortion or premature labor is less likely to ensue.

Acute surgical emergencies, however, must be treated immediately without thought of the pregnancy. The operative mortality is but slightly increased and the gross loss of fetal life averages only about 5 per cent. Abortions do not often occur unless the embryo is defective or the operation involves manipulation of the reproductive tract.

It may be worth while to administer corpus luteum hormone (progesterone), beginning a day or two before operation and continuing until convalescence is well established. The decrease in corpus luteum hormone secretion near the end of term and the increasing sensitivity of the uterus to the oxytocic posterior pituitary hormone at this time probably are factors in the initiation of labor. Since progesterone decreases uterine contractility and sensitivity to pituitary hormone, it is often useful in prophylaxis against premature induction of labor from abnormal stimulation. Similarly, progesterone may be of help in preventing abortion if a surgical procedure is performed on a patient during the third or fourth month of pregnancy. At this time, the function of secretion of this hormone normally is transferred from the corpus luteum of the ovary to the placenta, and transient or temporary deficiencies may occur physiologically. If no signs of threatened abortion or premature labor occur, progesterone, 5 mg. in oil intramuscularly or 20 mg. orally, either daily or every other day should suffice as a prophylactic measure. If uterine bleeding or uterine contractions begin, the dose should be doubled, intramuscular administration being preferred.

### References

1. Levy, D. M.: *Psychic Trauma of Operations in Children and Note on Combat Neurosis*, *Am. J. Dis. Child* 69: 7, 1945.
2. Donovan, E. J.: *Congenital Hypertrophic Pyloric Stenosis*, *Ann. Surg.* 121: 708, 1946.
3. Clagett, O. T.: *Surgical Treatment of Aged*, *Minnesota Med.* 26: 884, 1943.
4. Carp, L.: *Basic Principles in Geriatric Surgery*, *Ann. Surg.* 123: 1101, 1946.
5. Holinger, P. H.: *Bronchoscopy in Postoperative Pulmonary Complications*, *S. Clin. North America* 18: 237, 1938.
6. Meloney, F. L.: *Prophylactic and Active Use of Zinc Peroxide in Foul-Smelling Mouth and Neck Infections*, *Ann. Surg.* 107: 32, 1938.
7. Ravdin, I. S., Stengel, A. Jr., and Prushankin, M.: *Control of Hypoproteinemia in Surgical Patients*, *J. A. M. A.* 114: 107, 1940.

- 8 Elman, R. L.: *Parenteral Alimentation in Surgery*, New York, 1946, Paul B. Hoeber, Inc.
- 9 Goldzieher, J. W., and Popkin, G. L.: *Treatment of Headache With Intravenous Sodium Nicotinate*, *J. A. M. A.* 131: 103, 1946.
- 10 Dameshek, W.: *Medical Progress, Hematology*, *New England J. Med.* 232: 250, 280, 1945.
- 11 Castle, W. B., and Minot, G. R.: *Pathological Physiology and Clinical Description of the Anemias*, New York, 1936, Oxford University Press.
- 12 Berry, L. J., and Spies, T. D.: *The Present Status of Folic Acid*, *Blood* 1: 271, 1946.
- 13 Lewis, J. H., and others: *Relation of Certain Fractions of Plasma Globulins to Coagulation Defect in Hemophilia*, *Blood* 1: 166, 1946.
- 14 Quick, A. J.: *Clinical Application of Hippuric Acid and Prothrombin Tests*, *Am. J. Clin. Path.* 10: 222, 1940.
- 15 Quick, A. J.: *Clinical Significance of Prothrombin as a Factor in Hemorrhage*, *Pennsylvania M. J.* 43: 125, 1939.
- 16 Quick, A. J.: *The Hemorrhagic Diseases*, Springfield, Ill., 1942, Charles C. Thomas.
- 17 Allen, J. G., Julian, O. C., and Dragstedt, L. R.: *Use of Serial Dilutions in Determination of Prothrombin by One Stage Technic*, *Arch. Surg.* 41: 873, 1940.
- 18 Aggeler, P. M., Howard, J., Lucia, S. P., Clark, W., and Astaff, A.: *Standardization of Quick Prothrombin Test With Reference to Statistical Significance of Variations in Prothrombin Concentration With the Use of Stable Thromboplastin of High Potency*, *Blood* 1: 220, 1946.
- 19 Smith, H. P., Ziffren, S. E., Owen, C. A., and Hoffman, C. R.: *Clinical and Experimental Studies on Vitamin K*, *J. A. M. A.* 113: 380, 1939.
- 20 Allen, J. G., Bogardus, G., Jacobson, L. O., and Spurr, C. L.: *Some Observations on Bleeding Tendency in Thrombocytopenic Purpura*, *Ann. Int. Med.* 27: 382, 1947.

## CHAPTER 10

### ORGANIC DISEASES

While the medical management of surgical patients with coincidental heart disease, hypertension, nephritis, or diabetes should always be undertaken by an internist, it is important for the surgeon to have a clear understanding of all the therapeutic problems involved. The following brief discussion is offered to provide a summary of certain practical aspects of medical control of these organic diseases in surgical patients.

#### Cardiac Disease

Although experience has demonstrated that coincidental heart disease in a surgical patient does not necessarily add greatly to operative mortality, the increased risk involved usually is somewhat overemphasized. Consequently, a necessary operation is often delayed unduly long or, in many cases, is denied to a patient whose health might be improved and whose general outlook might be made brighter by the correction of some operable pathologic condition. Removal of a source of constant ill health, such as a chronically diseased gall bladder or an abdominal hernia, often not only will correct the local disturbance, but also will bring about marked improvement in the cardiac status. This effect has been brilliantly demonstrated by Lahey and Hurxthal<sup>1</sup> in thyrocardiac patients in whom the removal of the overactive thyroid gland has been followed by spectacular improvement in the heart failure, compensation being restored in practically all patients with congestive failure, and normal rhythm reappearing in nearly three-fourths of all patients with auricular fibrillation.

In view, therefore, of the small increase in operative mortality as a result of complicating heart disease, elective surgery should not be denied a patient whose general health might thereby be improved, without consideration of the type and prognosis of the cardiac lesion. The responsibility for the care of these individuals must be divided between the surgeon and a capable internist throughout the entire hospital course.

As a rule, if a patient's heart has sufficient reserve capacity to enable him to carry on his daily activities without much diffi-

culty, he can be subjected to anesthesia and operation with safety.<sup>2</sup> The signs and symptoms most generally useful in determining the functional capacity of the heart are the degree of fatigue noted on moderate exertion, the appearance of breathlessness or cardiac pain following exercise, the occurrence of dependent edema, and a history of nocturnal dyspnea. If none of these findings is present to a significant degree, either upon physical examination or in the history, the patient usually can be considered an acceptable operative risk, at least with respect to the heart lesion. The average patient, properly prepared for a surgical procedure, suffers little more cardiac strain from an operation skillfully performed under an expertly administered anesthetic than he would experience from the normal activity of an average day.

Determination of the extent and type of the cardiac damage should be approached from the standpoint not of the tabulation of physical signs but of the evaluation of cardiac reserve. Many people go through life as chronic invalids, believing that they have heart disease because of the presence of a systolic pulmonic or apical murmur. As an index of operability, physical signs are of much less importance than the degree of cardiac reserve. Finally, the expected improvement in health following operation should be balanced against the probable increase in operative risk. Obviously, a patient with coronary disease restricting his activities would prefer to wear a truss for a small hernia rather than to undergo operation.

Hamilton<sup>3</sup> states that, although about 7.5 per cent of all patients entering a general surgical clinic present points in their histories or physical examinations that arouse suspicion of cardiac disease, only 2 per cent of the total number actually have significant cardiac lesions. Organic heart disease, as a rule, should be diagnosed only when there is a history suggestive of previous cardiac failure, paroxysmal or nocturnal dyspnea, coronary disease, or anginal attacks or when the patient presents physical signs of cardiac or aortic enlargement, extracardiac evidences of developing cardiac incompetency, a serious disorder of rhythm, or marked hypertension, particularly of the diastolic level.

Butler, Feeney, and Levine<sup>4</sup> report that in 494 operations upon 414 patients with heart disease of all types, the total general mortality was 12.1 per cent. However, when inevitable deaths

were eliminated, such as those which occurred in patients already moribund from their cardiac or surgical conditions, and when only unexpected cardiac deaths were considered, the corrected mortality was only 6.3 per cent. Most of these deaths, furthermore, occurred in older patients.

### Minor Abnormalities.—

**FUNCTIONAL SYMPTOMS.**—Of the cardiac manifestations sometimes seen in nervous people or in those too long unaccustomed to physical exercise, the most important and most common is undue breathlessness on effort. This symptom differs from that occurring in a healthy individual following strenuous exercise only in the slight amount of exercise required to produce it and in its relative severity. It is most often noted in two types of people, those suffering from psychoneuroses of various sorts and those afflicted by a long-standing chronic infection or recuperating from a debilitating illness.

Characteristically, these patients are thin, pale, and nervous. The pulse and respiratory rates are normal during sleep, but they are definitely elevated while the patient is awake, even if he is at rest. Following slight exercise, however, the pulse and respiratory rates and the blood pressure increase out of all proportion to the degree of exertion. The pulse rate may rise from a resting basal rate of 90 or more to a peak of 140 to 180. Physical examination reveals no evidence of cardiac enlargement or organic cardiac disease. No basal râles in the lungs, no dependent edema, no nocturnal dyspnea, and no significant murmurs are present. After exercise the entire precordium moves diffusely with each beat of the heart, with no well-localized impulse, but the valve sounds, although somewhat slapping, are usually clear and sharp. A basal systolic murmur may appear at times, but it is not transmitted and not heard at the apex. The entire picture is that of an undernourished, emotionally unstable individual, too long unused to exercise, but organically sound.

Many of these patients have been told that they have heart disease; some have had digitalis; all are seriously hampered by their poor exercise tolerance and neurotic trend of mind. If possible, improvement in general health should be secured before operation. If emergency surgery is necessary, however, these



patients may be considered as normal risks with respect to their circulatory systems.

The excitement stage of anesthetic induction should be minimized by the preoperative administration of a barbiturate, such as Nembutal or Seconal, 0.2 Gm. (gr. 3), or a small dose of Avertin rectally (50 to 60 mg. per kilogram of body weight). Ether is the anesthetic of choice. During the postoperative period a persistently rapid pulse rate need cause no alarm as long as there are no signs of cardiac failure, and digitalis and other cardiac supportives should not be administered. No useful purpose will be served by decreasing the stroke volume and pulse rate by means of digitalis in an organically sound heart that is beating rapidly in response to an overactive nervous system. These remarks also hold true in the case of the patient who complains of "pain around the heart" without any relation to exercise; many times a direct relation to emotional instability may be perceived.

#### MINOR ARRHYTHMIAS.—

1. Of these less important pulse irregularities, the commonest is probably the occasional extrasystole or *premature contraction*. This is evidenced clinically by a premature beat followed by a prolonged pause, similar cycles occurring at irregular intervals and disappearing following exercise. The premature contraction may occur at entirely irregular intervals or in a rhythmic order, with coupled or tripled beats followed by a short pause. This complaint also is usually found in more or less nervous and emotional individuals, especially in young people of sedentary habits. The irregular beats may not produce any sensation, but, as a rule, the sufferer is likely to feel a flapping or thumping impulse in the chest, particularly when at rest. In this type of person, too, such a symptom is likely to produce considerable alarm.

Extrasystoles occasion no increased risk with respect to anesthesia and surgery if actual organic cardiac disease is not present also. *Extrasystoles alone*, even if they occur at frequent intervals, do not impair cardiac function and this fact might well be emphasized to the patient and the attendants. Frequently, proper regulation of the gastrointestinal tract, avoidance of stimulants, and restriction of smoking will decrease the severity of the cardiac complaint. In more severe cases adminis-

tration of sedatives or, as a last resort, of small doses of quinidine, for example, 0.2 Gm. (gr. 3) two or three times a day, may decrease the palpitation.

2. *Sinus arrhythmia* is frequent in children and elderly people. This irregularity accompanies deep breathing, appearing as an acceleration of the pulse with inspiration and a slowing of the pulse with expiration, the arrhythmia disappearing after exercise. Demonstration, by deep breathing, of its relation to the respiratory cycle will serve to distinguish it from abnormal arrhythmias, although it may exist in conjunction with unrelated heart disease. This arrhythmia also has no effect upon surgical risk.

3. At times, any individual's heart rate may be temporarily increased above the normal as a result of some *associated disease* not immediately apparent, such as latent hyperthyroidism, a hidden focus of infection, early pulmonary tuberculosis, alcoholism, anemia, avitaminosis, or an improperly adjusted emotional conflict.

These possibilities must be considered whenever a patient presents a persistent elevation of pulse rate without evidence of cardiac damage. In these cases the cardiac impulse is usually spread diffusely over the precordium and a soft systolic blow is often associated, particularly at the base of the heart. Such manifestations do not indicate cardiac disease and correction of the underlying cause will bring the pulse rate to normal. Sedatives, such as triple bromides or phenobarbital, will afford temporary relief. These patients offer no increased surgical risk because of the cardiac state itself.

Certain conditions may cause a decrease in pulse rate without associated heart disease. While hyperthyroidism and emotional strain are expected to be associated with a rapid pulse rate, it must be remembered that hypothyroidism and mental depression, on the contrary, may signal their presence by a decrease in pulse rate. Some individuals with increased vagal tone may suffer typical fainting attacks which are characterized by pallor, transient cerebral anemia, sweating, fall in pulse rate, and loss of consciousness of varying degree and duration. This condition need cause no alarm, even if it occurs before or after a surgical operation; it is simply a physical response to an emotional strain. Atropine sulfate, 0.8 mg. (gr. 1/75) hypodermically, usually will

release the vagal effect on the pulse, and aromatic spirits of ammonia or some other sharp sensory stimulation will restore the patient to consciousness.

4. *Paroxysmal tachycardia*, a common disorder of rhythm in which the pulse rate may rise suddenly to 150 to 200 per minute and within one to forty-eight hours revert as suddenly to normal rate, may be an alarming manifestation, particularly after operation, but it is of no serious import unless the heart is organically diseased or the condition is of long duration. This disorder often occurs in young or middle-aged people and occurs most frequently in persons without organic heart disease. No special preoperative precautions or preparations are necessary, and the occurrence of this rhythm disorder after operation, especially after urologic surgery, should not cause undue alarm. The condition may be abolished sometimes by sharp pressure on either carotid sinus region or on the eyeballs. Postoperative abdominal distention, particularly of the stomach, may precipitate it; appropriate treatment should be instituted either by gastric lavage or by enemas.

If the condition persists, the patient is propped up, sedatives are administered, and a liquid diet or light bland diet is ordered. Under such management, attacks of paroxysmal tachycardia may stop spontaneously after several hours. When there is no response to the simpler measures of treatment, more powerful drugs may be used. Quinidine sulfate probably is more effective than digitalis and is given in doses of 0.4 Gm. (gr. 6) every two hours for five doses, up to a total of 2.0 Gm. (gr. 30). If this dosage does not produce reversion to normal rhythm and further doses of quinidine are contemplated, the patient should be watched closely for symptomatic evidences of quinidine toxicity (cinchonism) and an electrocardiogram should be taken before each additional dose is given to prevent overdosage. Excess dosage of quinidine, administered after electrocardiographic evidence of toxicity has appeared, may induce ventricular fibrillation by profound depression of the conduction system.

Mecholyl (acetyl-beta-methylcholine), sometimes used in the treatment of paroxysmal tachycardia,<sup>8</sup> produces a reversion to normal cardiac rhythm through powerful stimulation of the vagus. Because of the general parasympathetic stimulation effected by this drug, unpleasant side effects are often present, in-

cluding flushing, sweating, palpitation, nausea, and perhaps even evacuation of the bowels. More severe toxic effects include vomiting and fainting; if these appear, atropine should be administered instantly. Mecholyl is given hypodermically in doses of 20 to 30 mg. (gr.  $1/3$  to  $1/2$ ). It is advisable to have a bedpan ready in case sudden evacuation of the bowels occurs and to have a hypodermic syringe containing atropine sulfate, 1.0 mg. (gr.  $1/60$ ), already prepared in case severe toxic effects should supervene. Mecholyl is a potentially dangerous drug and must be used with care; it must never be used in old people or in patients with angina pectoris or coronary sclerosis.

As a rule, simple measures of treatment suffice to restore normal rhythm in cases of paroxysmal tachycardia occurring before or after surgical operations; neither quinidine nor Mecholyl is necessary often.

### Major Abnormalities.—

#### MAJOR ARRHYTHMIAS.—

1. *Auricular flutter*, a relatively uncommon disorder of rhythm, is produced by an abnormal auricular contraction wave. It is manifested by an auricular contraction rate of 250 to 300 per minute with a varying degree of ventricular block. About one-half of these impulses produce a ventricular systole, the resulting rhythm often being irregular at intervals. This disorder is frequently associated with organic cardiac disease and is more likely to occur in older patients. Flutter may appear in attacks of short duration, but usually it persists for several weeks or longer. In this condition also the pulse rate may be slowed by pressure on the carotid sinus or on the eyeballs, but the effect lasts only for several seconds. This disorder is more serious and is more closely related to auricular fibrillation than is paroxysmal tachycardia, but it generally responds to therapy.

Quinidine has been advocated by many as a remedy for auricular flutter, but it is much less dependable in its results than digitalis, which is administered in doses of 0.2 Gm. (gr. 3) every 8 hours for two days, followed by a maintenance dose of 0.1 Gm. (gr.  $1\frac{1}{2}$ ) daily. When the ventricular rate approaches normal in response to digitalis, flutter is sometimes succeeded by fibrillation, which may revert to normal rhythm if the medica-

tion is stopped. One of the pure digitalis alkaloids (p. 245) may be used with equally good or perhaps better results; lanatoside C (Cedilanid), for example, may be slowly given intravenously in a dose of 0.8 mg. (4 c.c.) and repeated after four hours if necessary.

The various tachycardias, as a rule, can be differentiated by history and clinical manifestations. The electrocardiogram, however, affords a means of positive identification and should always be employed in every case of persisting tachycardia.

2. *Auricular fibrillation*, related to auricular flutter, produces an "irregular irregularity" in the pulse rate. The condition, in itself, is not a definite contraindication to surgical operation if it is properly handled; Butler and associates<sup>4</sup> report only a 3 per cent unexpected mortality in eighty-seven cases. However, auricular fibrillation should be considered as evidence of more serious cardiac disease until proved otherwise, although in many instances no organic basis for the arrhythmia can be demonstrated.

Some patients with congestive failure also exhibit auricular fibrillation and it is usually associated in young people with rheumatic valvular disease or severe hyperthyroidism. The best prognosis, particularly in cases likely to come to the attention of the surgeon, is offered by patients with hyperthyroidism, since the arrhythmia may disappear following thyroidectomy. In fact, auricular fibrillation in the presence of hyperthyroidism is more of an indication for operation than a contraindication (p. 739). If the cardiac reserve in a diseased heart is still at a fairly high level at the time of onset of fibrillation, the patient gradually develops decreasing exercise tolerance until dyspnea on slight exertion finally gives way to actual congestive failure. The condition is always most serious when it occurs in a patient with an already failing heart.

The arrhythmia should be controlled before operation is undertaken unless it is present in a thyrotoxic patient being prepared for thyroidectomy (p. 741). Auricular fibrillation developing as a postoperative complication in any case requires prompt and proper medical treatment. As in the case of any other form of heart disease in surgical patients, management of the cardiac disorder should be undertaken by an internist working in collaboration with the surgeon.

In general, the use of digitalis preparations is safer and more dependable than administration of quinidine for auricular fibrillation, digitalis being used to reduce the rate and quinidine to restore normal rhythm. Occasionally, however, auricular fibrillation occurring in the absence of pre-existing heart disease, especially in young people, will respond promptly to quinidine in relatively large doses. This drug should be given in auricular fibrillation only to restore normal rhythm and must not be used if there is any evidence of significant cardiac damage or of impending cardiac failure. It is given in doses of 0.4 Gm. (gr 6) every four hours for five doses daily for two days, a total of 2.0 Gm. (gr. 30) each day. This dosage may produce toxic effects; if reversion to normal rhythm has not occurred after the fifth dose has been given, an electrocardiogram should be taken before each succeeding dose and the patient should be watched for signs of cinchonism. The drug is discontinued if normal cardiac rhythm appears or if signs of toxicity develop either systemically or on electrocardiography. If quinidine is ineffective or if persistent auricular flutter develops following its use, the patient is given digitalis.

**CARDIAC VALVULAR DISEASE**—Patients with this type of heart lesion, in the absence of failure or a history of failure, present only a slight increase in mortality rate following major surgery. Several who have collected series of cases in which the patients had this type of cardiac disease state that the increase in operative mortality is slightly more than 2 per cent above the expected figure. Here again it may be repeated that it is not so much the type of valvular lesion present as the functional reserve of the heart that determines the condition of the patient. In this connection the history is of as much importance as the physical examination. Information of particular value includes a history of *previous congestive failure or paroxysmal nocturnal dyspnea*, a statement of how far the patient can walk or how many stairs he can climb without becoming dyspneic, and, finally, the proportion of an average daily life's activity he is able to perform. Satisfactory answers to these questions and satisfactory responses to simple exercise tests will yield more dependable information concerning the state of the cardiovascular system than a detailed anatomic investigation.

Preoperative preparation of a patient with this type of disease is more likely than any other to cause dissension between surgeon and medical consultant. Many men are inclined to administer digitalis routinely to all patients with cardiac lesions of any type. The only patients in whom digitalis may properly be used to advantage, however, are those with congestive failure with or without auricular fibrillation, those with auricular fibrillation alone, or those with auricular flutter. The drug may be actually harmful in unsuited cases, for in full therapeutic doses it may precipitate pulse irregularities or heart block, especially in patients with arteriosclerosis.<sup>4</sup> In patients in whom its use is not indicated, digitalis keeps the pulse rate at a low level and decreases the stroke volume, thereby maintaining the output per minute at a level below that which may be required physiologically. It will therefore not aid a heart that is maintaining the circulation at the best level that the lesion will permit nor is it a good prophylactic for ordinary arteriosclerotic patients. In small doses digitalis is probably of little use from any standpoint. For these reasons patients who present cardiac valvular disease without a history of cardiac failure or without clinical evidence of impaired cardiac reserve or early congestion may be considered to be ordinary standard operative risks and to require no special precautions beyond close attention in the postoperative period.

Patients who exhibit signs of beginning venous congestion, such as slight dependent edema, early basal rales, or a minor decrease in exercise tolerance, should be kept in bed on a light but high caloric diet, easily digested and relatively high in carbohydrate. No cardiac stimulants should be administered. Operation may be undertaken several days after all signs of congestion have disappeared. Preoperative medication in this type of case is probably best restricted to morphine, for the more powerful barbiturates are not advised for patients with cardiac disease, and tribromethanol (Avertin) may damage a congested, slightly anoxic liver.

Since valvular disease, especially mitral stenosis, is likely to induce an associated pulmonary passive congestion, the anesthetic chosen should be one that can be given together with a high concentration of oxygen. Ether is usually preferred, since it will produce no deleterious effect on a diseased heart, especially if administered as a vapor together with pure oxygen. It has,

however, a tendency to produce postoperative pulmonary congestion, particularly in aged patients, and prophylactic use of carbon dioxide inhalations and administration of pure oxygen during the immediate postoperative period are advisable.

Close watch must be kept upon these patients during the postoperative period so that early pulmonary complications may be detected and treated during the incipient stages. If fluids are given intravenously to a patient with heart disease, either before or after operation, the rate of administration should be slow, preferably not over 5 c.c. a minute, and evidences of cardiac embarrassment should be watched for during the treatment. The appearance of basal râles in the lungs or of signs of peripheral venous congestion requires the immediate discontinuance of the infusion. When a patient must be given an infusion and a gastric lavage at approximately the same time, the lavage should be performed before the blood volume is increased by the intravenous introduction of fluids.

**CONGESTIVE FAILURE.**—Patients who require surgery in the presence of cardiac failure with pulmonary or peripheral venous congestion require considerable thought and careful therapy. The precipitating factor responsible for the production of congestive failure must be recognized and treated, since the prognosis depends on the degree of damage to the heart muscle even more than on the type of anatomic lesion present. Congestive failure following, for example, an attack of influenza may disappear with the subsidence of the infection, but failure following pneumonia or an exacerbation of rheumatic fever is not likely to offer such a promising future. Similarly, congestive failure resulting from and present during an attack of auricular fibrillation is much more favorable in outlook than failure with a normal rhythm; with the correction or proper treatment of the arrhythmia the failure will often disappear.

If the surgical lesion will permit delay, the patient with congestive failure and normal rhythm should undergo a long period of preoperative preparation. While absolute bed rest is no longer considered advisable for cardiac failure, the patient is still forced to spend most of his time in the recumbent position. Breathlessness is diminished by elevation of the head of the bed, the elevation being adjusted to the position of optimum respiratory comfort for the patient. As a rule, recumbency is comfortable only when



dyspnea and pulmonary congestion are absent, when the patient has difficulty in breathing, he should be propped up constantly, either on a back rest or with the head end of the bed elevated. The attendants must be cautioned to keep the patient in this position even while he is being bathed; occasionally also an untrained person will lower the head of the bed while the patient is asleep in a misdirected effort to put him in a more comfortable position, whereupon he will awaken in fright with severe respiratory distress. Dyspnea in cardiac failure is due not only to pulmonary congestion and anoxemia, but also to constant and severe apprehension, which is of course greatly increased in surgical patients.

There has been a trend recently to increase the amount of exercise permitted<sup>1,2</sup> for patients in cardiac failure, both to minimize the danger of venous thrombosis and pulmonary embolism and to maintain the patient's general strength and optimistic outlook.

Cough due to pulmonary congestion may be treated with frequent small doses of codeine, 16 to 32 mg. (gr.  $\frac{1}{4}$  to  $\frac{1}{2}$ ); cough due to bronchitis is best treated with an expectorant mixture. Cardiac patients often have much difficulty in sleeping, and some mild sedative such as ammonium bromide, 1 to 2 Gm. (gr. 15 to 30), with chloral hydrate, 0.6 to 2.0 Gm. (gr. 10 to 30), or paraldehyde,  $\frac{1}{2}$  to 16 c.c. (dr 1 to 4), may be used. In more severe cases, morphine, 10 to 16 mg. (gr.  $\frac{1}{6}$  to  $\frac{1}{4}$ ), may be necessary, but repeated doses of this drug must be used with some caution in the presence of pulmonary congestion and edema.

When kidney function is unimpaired, there seems to be no need to restrict salt-free fluids, even in patients with congestive failure. In fact, increased intake of pure water or dextrose (5 per cent) solution actually may effect a reduction of edema<sup>3</sup> by promoting excretion of some of the retained salt through the kidneys. The Karell diet (nothing by mouth except 200 c.c. of skim milk every four hours four times daily) is no longer used much, because the fluid restriction is unnecessarily severe and because even skim milk contains an appreciable amount of salt. In all patients with congestive failure, whether early or advanced, salt in the diet must be kept at a minimum. Diet should be as light as possible; as a matter of fact, the patient is often too uncomfortable to desire food. The bowel movements should be

kept semisolid by administration of small doses of saline cathartics, although liquid stools are not desirable because of their weakening effect.

Generalized edema, particularly noted in the legs, decreases rapidly following full digitalization and institution of other therapeutic measures for congestive heart failure. During this period a scrotal support will help to prevent extensive local edema. Diuretic drugs are of considerable value in hastening the disappearance of edema fluid. Although extensively used in the past, xanthine drugs such as aminophylline, theophylline, and theobromine calcium salicylate are no longer employed widely as diuretics since they are not dependably effective alone and are likely to induce nausea and vomiting. Ammonium chloride, administered as enteric-coated tablets in doses of 1 to 2 Gm. (gr. 15 to 30) four times daily, is fairly effective as a diuretic and also induces an acid reaction in the urine, which enhances the diuretic action of the mercurial drugs usually given in conjunction with it. The most widely used mercurial diuretics are Salyrgan-theophylline, Mercuhydrin, and Mercupurin, given intramuscularly in doses of 1 to 2 c.c. of 10 per cent solution at intervals of several days, preferably in the morning. Batterman and co-workers<sup>10</sup> suggest the use of Mercupurin orally, either as a single dose of 5 tablets or in a dose of 2 tablets three times a day for several days. Salyrgan also is effective when given orally in tablet form.

Edema due to cardiac failure affords the strongest indication for the use of mercurial diuretics, but since these compounds tend to aggravate any existing lesion of the kidneys, their administration should not be repeated if evidences of renal irritation develop.

Patients with congestive heart failure may develop sudden attacks of acute paroxysmal dyspnea at any time. These episodes may or may not be accompanied by well-defined asthma with expiratory dyspnea and are characterized by extreme discomfort and apprehension. Prompt treatment is necessary; continuance of the attack may be followed by pulmonary edema. Acute paroxysmal dyspnea in these patients is based upon the marked decrease in vital capacity consequent to heart failure; minimal stimuli which ordinarily would cause only a small increase in ventilation will precipitate respiratory insufficiency in the con-

gested lungs of the patient with cardiac failure. Such precipitating factors include sudden emotion, changes in position while asleep, a heavy meal, abdominal distention, attacks of coughing, and similar occurrences that may not be preventable even by expert nursing care. Once begun, the attack is always made more severe by the excitement and apprehension produced in the patient.

Treatment of paroxysmal dyspnea includes prompt elevation of the patient to a sitting or semisitting position and administration of morphine, 16 mg. (gr.  $\frac{1}{4}$ ) hypodermically or 10 mg. (gr.  $\frac{1}{6}$ ) intravenously. The use of atropine, 0.6 mg. (gr.  $\frac{1}{100}$ ), together with morphine is advised by some. The chief value of morphine in such cases lies not only in the relief of respiratory distress but in the relief of the patient's excitement and fright. If severe asthma is present, the use of morphine is inadvisable, just as in asthma due to any other cause. In such patients aminophylline is the drug of choice and usually will produce prompt relief. Aminophylline is given intravenously in a dose of 0.24 Gm. (gr.  $\frac{3}{4}$ ), from three to five minutes being required to complete the injection. When relief is insufficient or previous experience has indicated that a larger dose is necessary, aminophylline, 0.5 Gm. (gr.  $\frac{7}{12}$ ), is given intravenously over a fifteen- to twenty-minute period, preferably in at least 100 c.c. of fluid by intravenous drip. Aminophylline is also the proper drug for use if Cheyne-Stokes respiration is present; the depressant effect of morphine makes its use dangerous under those circumstances. Oxygen administration by means of a tent is often of value and occasionally even venesection may be required in treatment of acute paroxysmal dyspnea due to cardiac failure.

Steps taken to decrease the likelihood of further attacks include proper digitalization, use of diuretics, restriction of salt, use of sedatives, attention to the diet and elimination, maintenance of a propped-up position during sleep, and perhaps the administration of aminophylline for prophylaxis in doses of 0.1 to 0.2 Gm. (gr.  $1\frac{1}{2}$  to 3) orally three times a day or as a suppository or retention enema in water in twice this dosage once in the evening.

Patients in whom cardiac failure is so marked that collections of fluid occur in the serous cavities are not likely to find their way into the care of a surgeon, although the possibility of

a pleural or peritoneal transudation in postoperative cardiac failure must be remembered. These patients usually are too severely ill to recover, but removal of the fluid by aspiration will add to their comfort temporarily.

Venesection is often useful as an emergency procedure to produce a decrease in venous pressure and a reduction in viscosity of the blood by its consequent dilution with tissue fluid transudate. The usual amount of blood withdrawn is 250 to 500 c.c., depending upon the degree of congestion, and withdrawal should be done rapidly. This form of therapy is strictly one to be carried out by the medical consultant, since a patient so severely ill should by all means have an internist's continuous care. Venesection is generally employed in conjunction with rapid digitalization or with the intravenous administration of strophanthin (p. 246). Since the cardiac problem in these individuals is more of a mechanical than a chemical one, oxygen supplied by means of an intranasal catheter or an oxygen tent has been somewhat disappointing, although a little beneficial effect is sometimes noted in severe cases.

When auricular fibrillation is present in association with congestive failure, the general plan of treatment is the same. Digitalis, as previously mentioned, is indicated in the treatment of congestive heart failure and in restoration of normal rhythm in patients with persistent major arrhythmias but is not indicated as a cardiac tonic in patients with well-compensated heart disease, either before or after operation.

Digitalis produces several effects upon the heart. One of the chief actions of the drug is to decrease the conductivity of the auriculoventricular bundle and its branches, diminishing the number of impulses reaching the ventricle. Other effects of digitalis include depression of pacemaking activity at both the sinoauricular and auriculoventricular nodes, lengthening of the refractory period of both the auricular and the ventricular cardiac muscle, and improvement in cardiac muscle tone and efficiency of contraction. These effects result in improvement of the contractile power of the failing muscle, increased rest periods for the heart, decreased energy output, and increased diastolic filling of the ventricle. Constant clinical benefit can be expected only when full therapeutic doses are given; small daily doses are believed by many to produce tonic effects, but these are incon-

stant unless use of the drug is indicated clinically and it is given in dosage approaching the theoretic optimum.

Full dosage of digitalis generally is considered to require about 0.06 to 0.1 Gm. (gr. 1 to  $1\frac{1}{2}$ ) of the powdered leaf (U. S. P. XII, 1942) for each ten pounds of body weight plus 0.06 to 0.1 Gm. for each day required to build the dosage to the optimum. The necessary amount varies somewhat in different individuals, and it may be simpler to consider the administration of a total of 1.5 Gm. of digitalis (powdered leaf) in a period of twenty-four hours as full digitalization. Once the proper clinical effect has been obtained, a daily dose of 0.1 Gm. (gr.  $1\frac{1}{2}$ ) of the powdered leaf is sufficient as a rule to maintain digitalization.

In treatment of patients with cardiac failure and auricular fibrillation, some authorities prefer to administer digitalis until the pulse rate drops to the desired level of 70 to 80 per minute, or until toxic manifestations appear, such as nausea and vomiting, diarrhea, or coupled beats. Occasionally, cardiac failure may be present with a normal pulse rate; in such individuals digitalis may effect full clinical improvement without any alteration of pulse rate and without production of toxic symptoms. The effects of digitalis are cumulative; little benefit is produced until the heart muscle has reached a proper degree of saturation with the drug and, conversely, withdrawal of the drug and physiologic excretion of any excess will cause toxic symptoms to disappear.

Digitalis is administered according to the requirements of the individual. Before any of the digitalis group of drugs is given, one should know if the patient has received digitalis before admission, when it was given, and in what doses it was given.

Patients requiring rapid treatment can be given one-half the calculated total dose at one time and the remaining one-half in fractional doses to cover twenty-four hours. By another plan, 0.3 Gm. (gr.  $4\frac{1}{2}$ ) of digitalis can be given every eight hours for three or four doses to attain full digitalization in twenty-four to thirty-two hours. Administration of the total dose should not be attempted in less than twenty-four hours when digitalis leaf is used, nor should doses be given more often than every four or preferably every six hours. Obviously the dosage calculated according to weight is merely a rough approximation, the

degree of edema and the amount of obesity providing sources of error. If, however, the desired effect is produced by the aforementioned dosage, administration of an average maintenance dose of 0.1 Gm. (gr.  $1\frac{1}{2}$ ) daily to replace the amount excreted will maintain the full effect of the digitalis.

When failure is less severe, the drug may be given more slowly. In such a case, 0.2 Gm. (gr. 3) of digitalis leaf is given every eight hours for six or seven doses, requiring two days for full dosage, or 0.1 Gm. (gr.  $1\frac{1}{2}$ ) may be given three times a day for four to five days. Prolongation of the period of digitalization reduces the occurrence of toxic symptoms.

Sudden or extreme degrees of cardiac failure may require the utmost rapidity in supplying supportive treatment. Purified preparations of digitalis alkaloids now available can accomplish full digitalization with a single dose or with two doses of the drug administered either orally or parenterally. Digitoxin, a purified cardiotonic glycoside derived from *Digitalis purpurea*, has 1,000 times the activity of standard digitalis powdered leaf on the basis of oral administration. An oral dose of 0.1 mg. of digitoxin is equivalent in therapeutic effect to 0.1 Gm. of digitalis leaf. Since it is absorbed rapidly and practically completely following administration by mouth, a single oral dose of 1.2 to 1.5 mg. of digitoxin will produce full digitalization within a period of six to eight hours, or an equivalent total amount may be given in divided doses of 0.2 to 0.5 mg. over a period of twenty-four hours. The daily maintenance dose is 0.1 to 0.3 milligram.

Pure glycosides are also available commercially in solution for intravenous injection in emergencies or when oral administration is not possible. Digitaline Nativelle (digitoxin) is given by vein very slowly in doses of 0.2 to 0.4 mg., repeated as necessary to accomplish digitalization over a period of twelve to twenty-four hours. The daily maintenance dose is 0.1 to 0.3 mg. and may be given orally. Lanatoside C, obtainable as Cedilanid, is one of the pure effective glycosides derived from *Digitalis lanata* and can be slowly given intravenously in a dose of 0.8 mg. (4 c.c.), repeated after four to eight hours for rapid digitalization. The two latter pure glycoside drugs can be given by mouth as well as by vein, but their greatest value perhaps lies in their availability for rapid therapy by parenteral injection. Cedilanid is preferable in dire emergencies, since it

acts more rapidly, producing its effect within two to three hours. Digitoxin, while just as effective therapeutically, acts more slowly, requiring from six to eight hours to produce digitalization. Digitoxin also is excreted more slowly than Cedilanid and consequently may be more likely to cause cumulative toxic effects. Other preparations of the same or similar drugs are available under different proprietary names. Slow digitalization is preferable when possible, however; purified drugs sometimes produce toxic effects due to rapid or excess dosage.

Some clinicians feel that strophanthin G (ouabain) may be somewhat more effective and more prompt in action than the digitalis alkaloids in stimulating an acutely failing heart. A dose of 0.25 to 0.5 mg. is given very slowly by intravenous injection, a noticeable effect usually appearing within one to two hours. A single dose<sup>11</sup> of the medication is sufficient as a rule, although it may be repeated after twelve hours if necessary. Strophanthin is never given to a patient who has had digitalis within the preceding week unless proper allowances are made in the size of the dose. When this drug has been used as an emergency measure to restore cardiac efficiency as rapidly as possible and it is desired to substitute a digitalis preparation after the acute heart failure has been controlled, the change in drugs can be made by beginning administration of digitalis orally within twelve hours after injection of strophanthin. The usual mode of relatively rapid digitalization can be followed; for example, 0.2 Gm. (gr. 3) of powdered leaf every eight hours for two days, with a maintenance dose of 0.1 Gm. (gr. 1½) daily thereafter.

**SYPHILITIC HEART DISEASE.**—This disease is commoner than is generally believed and accounts for a large percentage of cases of cardiovascular disease. Pathologic effects of the syphilitic infection consist chiefly of the destruction of the medial coat of the aorta, distortion of the aortic valve cusps, and narrowing of the mouths of the coronary vessels. The cardiac reserve decreases rapidly with the duration of the disease but can be improved by the usual measures if myocardial function is fairly good and aortic disease is not far advanced. In general, however, these patients are not as good surgical risks as patients with other types of cardiac disease of corresponding degree. Spinal anesthesia is especially dangerous in patients with syphilitic

aortitis and low diastolic pressure, because the fall in blood pressure following anesthesia may decrease the coronary blood flow enough to cause sudden death.

**CORONARY THROMBOSIS.**—This type of cardiac lesion produces the highest mortality of all, just as it is responsible for the most marked increase over the normal standard risk for surgical patients.

Often presenting symptoms strongly resembling those typical of various acute surgical diseases of the upper abdomen, acute coronary thrombosis may be responsible for fruitless surgical explorations, with fatal results. Butler, Feeney, and Levine<sup>4</sup> report five patients with undiagnosed acute coronary thrombosis who were subjected to operation during attacks, with four deaths. In case of doubt an electrocardiogram may decide the diagnosis. Patients who have had attacks and have regained a reasonable degree of health following fibrosis and healing of the infarct over a period of months may be subjected to necessary surgical procedures, although the operative risk is still very definitely increased and the added mortality is usually reported to be at least 15 per cent. Careful watching and expert nursing care are indispensable in these patients.

If a sudden attack of coronary occlusion develops, emergency care includes the administration of morphine, 16 to 32 mg. (gr. 1/4 to 1/2) hypodermically or 8 to 10 mg. (gr. 1/8 to 1/6) intravenously, absolute bed rest with the patient forbidden to make the slightest move without help, and installation of an oxygen tent. The use of nitroglycerin or of any vasodilator is not advocated in emergency treatment of coronary occlusion because of the danger of precipitating vascular collapse. Further treatment of coronary thrombosis is entirely in the realm of the internist; a patient who has had a recent attack of this type is not suitable for even an emergency operation.

In a report from the Mayo Clinic, Brumm and Willius<sup>12</sup> state that only 11 (4.3 per cent) of a series of 257 surgical patients with severe coronary disease died from purely cardiac causes following operation. Of these patients, 100 exhibited hypertension and 32 gave a history of previous coronary thrombosis. The average age of the patients in this series was 60 years and anginal symptoms had been present for an average of three years.



The unusually low associated mortality in this group of cases indicates the excellent results that may be expected from the proper care and management of the surgical cardiac patient.

**ANGINA PECTORIS**—With its almost constantly associated coronary arterial disease, angina pectoris increases the surgical mortality by about 8 per cent. Several series of cases of this type have been reported, with widely varying postoperative mortality percentages, although all authors agree that the added risk is serious. If operation is indicated in spite of the coincidental disease, all sources of excitement should be avoided, preoperative sedation with phenobarbital or Seconal should be effected, and a basal anesthetic, such as Avertin per rectum, should be given. If an ether anesthetic is administered skillfully and the operation is performed rapidly yet gently, the increased risk should not be prohibitive. Spinal anesthesia is distinctly contraindicated in patients with coronary or anginal disease just as it is in hypertensive heart disease, since the accompanying fall in blood pressure may have disastrous effects.

If anginal attacks supervene, a vasodilator drug must be given promptly. The most rapidly effective drug of this class is amyl nitrite, which is administered in doses of 0.18 to 0.31 c.c. (minims 3 to 5) by inhalation from a glass ampule or "pearl" crushed in a handkerchief or gauze sponge. An instantaneous and marked drop in blood pressure occurs, lasting for several minutes, together with an effective dilatation of the coronary vessels. Nitroglycerin also is given for this purpose in the form of a tablet containing 0.6 mg. (gr. 1/100) of the drug placed beneath the tongue to insure rapid direct absorption. The resulting vasodilatation appears within two minutes and persists for approximately half an hour. This drug may be of value in averting possible attacks of anginal pain if given in doses of 0.12 to 0.3 mg. (gr. 1/500 to 1/200) several minutes before a disagreeable treatment (gastric lavage, gastrointestinal x-ray, etc.) is performed. In addition to the usual preoperative medication in patients subject to anginal attacks, it may be worth while to administer nitroglycerin, 0.3 mg. (gr. 1/200) sublingually, five minutes before induction of anesthesia is started. Patients with moderately severe angina may be benefited by administration of small doses of nitroglycerin, for example, 0.12 mg. (gr. 1/500) every two or

three hours, during the waking hours of the day before and the day after operation.

Other vasodilator drugs are of less use in the symptomatic management of surgical patients with angina pectoris. For prolonged effect, erythrol tetranitrate is often used in oral doses of 32 to 64 mg. (gr. 1/2 to 1), producing a drop in blood pressure which develops in from twenty to thirty minutes and lasts for several hours. Any drug of the vasodilator class is likely to induce a headache in a susceptible individual. While vasodilator drugs are of specific value in relieving pain due to angina pectoris, their use is strongly contraindicated in the presence of coronary occlusion, in which a sudden fall in blood pressure might prove fatal.

**ANEMIA.**—In Negro patients, especially children, sickle-cell anemia may be responsible for acute hemoclastic crises following operation. This occurrence can be foreseen by the performance of a sickling test on the blood of any Negro patient in whom the possibility of this disease is considered. Treatment, of course, is transfusion of whole blood before and after operation. Anemia of any type will often produce a rapid pulse rate, poor exercise tolerance, and a systolic blowing murmur at the pulmonic area or at the apex. These manifestations disappear after correction of the deficiency. Patients with anemia should be given whole blood transfusions until the hemoglobin and red cell count have reached satisfactory minimum levels (p. 143) before operation is performed. Such patients also should receive oxygen in high concentration during anesthesia and operation.

### Essential Hypertension

Essential hypertension, the pathogenesis of which is still unexplained, is characterized by progressive narrowing of the arterioles throughout the body. As a result of the increased vascular resistance, the systemic arterial pressure is proportionately elevated. The physiologic basis of the arteriolar occlusion is thought to be a persistent spasm of these vessels, the smooth muscle of which is progressively replaced by connective tissue, so that the pathologic change becomes an irreversible one. Since the vascular changes are generalized, characteristic impairment of visceral function can be expected as a result of the consequent

agent. Spinal anesthesia is never employed in hypertensive patients, the resulting fall in blood pressure might be dangerous.

Hypertensive patients tend to bleed somewhat excessively during operation and also are likely to develop postoperative hematomas. Postoperative shock is fairly common because of the impairment of cerebral circulation caused by the drop in blood pressure during and after operation. The critical level of blood pressure at which shock appears is much higher in a hypertensive patient than in the patient with normal blood pressure. Because of the generally decreased capacity of the arteriolar bed, symptoms of anoxemia appear in such a patient before the falling blood pressure has dropped to an obviously low level. Intravenous fluids, when indicated, must be given slowly and in relatively small amounts to avoid the sudden overloading of a damaged circulatory apparatus. The infusion can be repeated as necessary.

Vasopressor drugs are to be used with caution in the treatment of postoperative shock in hypertensive patients, since peripheral vasoconstriction superimposed upon an already impaired circulation may tend to decrease tissue oxygenation even further. The mainstay of the treatment of shock is always the restoration of the blood volume, which is best accomplished by transfusion of whole blood or plasma. The possible effects of a sudden rise in blood pressure upon structurally damaged blood vessels are also to be considered when vasopressor drugs are employed. For the same reason the use of peristaltic stimulants that cause an accessory rise in blood pressure must be avoided after operation. Postoperative coronary thrombosis and cerebral hemorrhage are distinct dangers in old hypertensive patients with long-standing arterial disease. Any medication that may cause an incidental elevation of blood pressure must be used with caution, no matter what the purpose for which it is intended.

Hypertensive patients with cardiac enlargement and evidences of beginning failure must be prepared for operation as outlined in the preceding section. If signs of heart failure should appear in the hypertensive subject, the added surgical risk due to the cardiovascular disease is increased greatly. Such patients should be assured as long a period of bed rest as necessary before operation, with prescription of a light, easily digested diet and moderate restriction of salt. Digitalis therapy is administered

before operation if evidences of cardiac incompetency are present, and rapid digitalization is accomplished if the patient shows evidence of heart failure beginning immediately after operation. Mercurial diuretics may be used in treatment of cardiac edema in this type of patient provided no impairment of renal function is present. Codeine and sometimes morphine may be needed as adjuncts to sedation in assuring rest and relaxation if cardiac complications develop.

The not infrequent association of asymptomatic coronary disease with hypertension should also be remembered. The degree of risk involved in surgical procedures upon such patients depends upon the duration of the hypertension and the extent of consequent vascular and visceral damage rather than upon the actual blood pressure itself. A high blood pressure with early and minimal vascular change imposes less added surgical risk than a lower pressure level with marked involvement of the renal, myocardial, or cerebral vessels. Electrocardiographic and x-ray studies of the heart are of great prognostic value in these patients, as mentioned previously, and should never be omitted if the vascular disease is well established.

### Nephritis

The proper functioning of the kidneys, which are the chief agents for preservation of normal water and salt balance, for excretion of certain metabolic end products, and for excretory regulation of blood pH, must be maintained in order to carry the surgical patient safely through the usual postoperative period of disturbed metabolism. Any deficiency in renal function must be carefully estimated according to the past history of nephritis and the present evidence of damage. The presence of significant disease necessitates the cooperation of a qualified internist in the care of the patient throughout his course.

Of the various forms of kidney disease, the following are the most frequently encountered:

Renal arteriosclerosis, which is associated with essential or benign hypertension, does not usually produce enough glomerular damage to cause significant renal insufficiency. The characteristic pathologic change in the kidneys, as elsewhere in the vascular system, is the development of fibrosis and thickening

of the arteriolar walls, with progressive obliteration of their lumina and consequent reduction in glomerular circulation. The chief consideration, from the standpoint of the surgeon, is the degree of hypertension and possible associated heart disease rather than the renal changes. On the other hand, the drop in systemic blood pressure that usually occurs after any operation may cause such a sudden decrease in the glomerular blood supply that transient damage by ischemia may occur in arteriosclerotic kidneys, as evidenced by albuminuria of short duration after recovery.

**Acute glomerulonephritis** contraindicates operation for any reason but actually to save life. The disease usually follows one to two weeks after a streptococcus infection, such as tonsillitis, pharyngitis, scarlet fever, or mitis media, but occasionally there may be no evidence of antecedent infection. Recovery occurs within one to six weeks and is attended by disappearance of the rise in blood pressure, edema, oliguria, and hematuria, although albuminuria may persist for some time to testify to a persisting renal involvement. Those who do not recover from the acute disease die either immediately from acute vascular damage in the heart, kidneys, or brain or within three to twelve months as a result of permanent renal insufficiency due to hyalinization and obliteration of the glomeruli.

**Chronic Glomerulonephritis.**—A variable degree of permanent residual kidney damage follows the subsidence of the acute disease. A kidney thus affected shows destruction of many glomeruli. Some are completely hyalinized and scarred, while others are obliterated to a variable degree by crescentic overgrowth of the capsular epithelium, with an associated decrease in functional capacity. The unaffected glomeruli with their tubules are usually hypertrophied and dilated as a response to the increased work. Recurrent attacks of nephritis, marked clinically by edema, slight hematuria, and a slight rise in blood pressure, may further decrease the number of functioning units.

The matter of chief concern from the standpoint of the surgeon is the reserve capacity of the kidney, which depends directly upon the number of normally functioning glomerular units remaining. Since albuminuria may be the only overt evidence of renal damage, its discovery in a surgical patient calls

for a thorough investigation of the history for evidence of previous renal disease and of the urinary tract for determination of the present functional status.

The presence of albuminuria is of no diagnostic value with respect to the identification of the type of kidney disease present; this finding simply indicates the possible existence of renal damage. Classification of the renal lesion, however, is of much less importance to the surgeon than the determination of the functional capacity of the kidneys. Although there may be sufficient pathologic change in the renal arterioles in patients with essential hypertension to produce a slight degree of albuminuria with no significant impairment of renal function, true glomerulonephritis may be present in a hypertensive individual as well as in a person with normal blood pressure. As a general rule, in those patients who have had actual nephritis with residual chronic damage the albuminuria is more marked, the blood pressure, although elevated, is not necessarily much above normal, and old nephritic changes are sometimes evident in the eye grounds. The total daily urinary output is often increased, with a specific gravity more or less fixed at a low dilution (1.015 or below). Excretion in these patients continues at an undiminished rate through the night.

Nephritic patients exhibit a definite increase in susceptibility to infection. Respiratory infections are especially common and are likely to develop to serious proportions. Oral infections often occur. Progress of an infection may be accompanied by functional failure of the low reserve kidneys as a result of the added strain, and a postoperative complicating respiratory infection, which might be relatively easy to control in a patient with unimpaired renal function, may end in renal failure, nitrogen retention, and uremia in an individual afflicted with chronic nephritis.

Preoperative investigation of a patient with the possibility of nephritis should include examination of the urine for albumin, red blood cells, and casts, blood chemistry determination for evidence of nitrogen retention, and hemoglobin estimation and red cell count for the usually associated anemia. The renal reserve can be estimated fairly accurately by tests of the ability of the kidneys to concentrate and dilute the urine and by selective excretion tests.

### Examination of Urine.—

**ALBUMINURIA**—Following the passage of plasma protein through a partially damaged glomerular membrane, albuminuria appears. This nonspecific finding is present in all types of kidney disease as well as in fevers, marked anemia, and certain types of poisoning. It is also observed following alterations in the renal blood flow, as after crushing injuries, transfusion reactions, shock, sudden changes in blood pressure, severe exercise, or a sudden chill. The degree of albuminuria is directly proportional to the degree of damage to the glomerular membrane. During an attack of acute nephritis the plasma albumin, because of its relatively small molecule, may filter through the diseased glomeruli at a rate as high as 20 to 25 Gm. a day, leaving the globulin behind in the blood stream. Excretion of albumin may persist to some degree for months following an attack of acute nephritis and it always accompanies chronic kidney disease. A variable but usually small degree of albuminuria may be present also in essential hypertension, with no significant impairment of kidney function and without a history suggesting glomerulonephritis, although late in the course of the disease more pronounced renal changes are likely to develop.

*Orthostatic albuminuria* occurs at times in children and young adults and is usually associated with lumbar lordosis. In these patients the renal function itself is not impaired; the distinction from true kidney disease may be made by having the patient void while recumbent, about one-half hour after retiring, then again while recumbent before arising in the morning. The morning specimen should contain no albumin.

**CASTS**.—Casts are formed by the precipitation of the protein in the glomerular filtrate during its passage through the uriniferous tubules, in which concentration of the urine normally takes place by selective absorption through the lining cells. Urine which carries a high protein content for any reason at all is, therefore, likely to contain hyaline or granular casts. On the other hand, casts containing red blood cells indicate hematuria and casts containing renal cells signify parenchymal damage.

**HEMATURIA**.—This condition is produced only by actual rupture of the glomerular vessels as the result of glomerulonephritis, infarction, or congestive heart failure. Red cells may be

found occasionally in normal urine or in greater numbers in the presence of urinary tract infection, stone, tumor, ureteral stricture, or the interstitial cystitis of Hunner.

**POLYURIA.**—Fixed low specific gravity of the urine and polyuria appear as the result of destruction of many glomerular units. The remaining glomeruli are overactive as a consequence and secrete urine so rapidly that the speed of flow through the tubules becomes too great to permit proper concentration. As the kidneys become less able to excrete the salts and metabolic end products which normally pass out through the urine, the fluid and electrolyte balances are disturbed and retention edema appears in the body tissues, proportionate in degree to the kidney incapacity.

### Renal Function Tests.—

**URINARY CONCENTRATION TEST.**—The Mosenthal test as modified by Fishberg<sup>13</sup> is the simplest and most valuable of the renal function tests. The patient takes no fluids from lunch time one day until completion of the test two hours after awakening the next morning. Lunch and supper are taken as usual, but the evening meal includes no fluids. Nothing is taken by mouth the following morning until after the test is concluded. The urine voided before retiring is discarded. The patient voids on awakening in the morning, one hour later, and again another hour later, each specimen being collected in a separate bottle. The test is completed simply by the determination of the specific gravity of each of the three specimens, at least one of which should show a reading of 1.022 or over, greater concentration ability being normally noted in the young. Inability of the kidneys to concentrate the urine at least to this point indicates impairment of renal function, the degree of deficiency being roughly proportionate to the maximum degree of concentration. The test should not be performed during subsidence of edema, for the elimination of fluid from the tissues will influence the urinary concentration. This test is the most effective method of measuring the renal reserve, since an early impairment of kidney function can be demonstrated by this means before clinical evidences of renal damage appear.

**PHENOLSULFONPHTHALEIN EXCRETION TEST.**—Phenolsulfonphthalein is excreted rapidly and almost completely through the kidneys and the amount excreted can be determined colori-



metrically with ease. The test is usually performed by the intravenous injection of 1 c.c. (6 mg.) of the dye, about ten minutes after the patient has voided; one or two glasses of water are then given. The patient empties his bladder one-half hour after the injection of the dye, one-half hour later, and again one hour later, three specimens being collected. The most important of these is the first half-hour specimen. The dye content of each of the three specimens is estimated colorimetrically after the volume has been measured. Ordinarily 40 to 60 per cent of the dye is excreted in the first half-hour and 20 to 30 per cent in the remainder of the two-hour period. In some clinics the time at which the dye appears in the urine is noted, but this necessitates the introduction of a bladder catheter. Differential determination of the function of each kidney may be made, if indicated, by means of ureteral catheters.

The value of the phenolsulfonphthalein excretion test is lessened by the fact that the dye output may be within the normal range if renal deficiency is present but well compensated, even though the ability of the kidneys to concentrate is impaired. Excess administration of fluids during the dye excretion period may also result in an excessively increased output of the substance; not more than two glasses of water should be given during this time.

**STUDY OF CONSTITUENTS OF BLOOD.**—In the absence of extrarenal pathologic states, such studies will reveal the existence of decompensated kidney function. They will not, however, reveal any decrease in the renal reserve while the renal function is still sufficient to permit normal excretion under ordinary circumstances. Urinary constituents do not accumulate in the blood under usual conditions unless actual renal insufficiency is present. Significant elevations of the urea, nonprotein nitrogen, and creatinine of the blood indicate an inability of the kidneys to maintain satisfactory excretory function. Little information concerning the state of the kidneys can be gained by determination of the concentration of other blood components.

**UREA CLEARANCE DETERMINATION.**—This test, devised by Van Slyke and associates,<sup>14</sup> is a method of measuring the volume of blood cleared of urea by the kidneys within the space of one minute. As the renal function decreases, the clearance value

decreases sharply. This test is not difficult to perform and will reveal accurately the presence of kidney damage, unless there is a polyuria, which occasions the rapid excretion of a urine of low specific gravity.

**Special Measures.**—Special measures to be taken in case of the preoperative discovery of the presence of nephritis in a surgical patient depend on the stage and severity of the complication. Even if renal function is impaired, with inability to concentrate the urine to a satisfactory degree, fluids should not be restricted but on the contrary should be forced, with restriction of salt intake. The diet should be light and easily digestible and may contain protein in moderate amounts (50 to 60 Gm. per day). The protein may be of any type, no one form of meat being more harmful than any other. When significant amounts of protein are being lost in the urine, the addition to the diet of intermediate nourishments containing one or more ounces of low-salt content protein or protein hydrolysate preparations may help to compensate for the protein losses. Excess salt should be avoided; the diet should contain only the average amount used in cooking, no free salt being added later. No difficulty is usually experienced in the management of this type of patient if a close watch is kept upon the urinary output, the salt intake, the degree of urinary concentration, and the level of the blood urea. Operation is never undertaken upon a nephritic patient if the urinary output is low, especially if the specific gravity of the urine also is low.

In the nephrotic type of glomerulonephritis with pronounced albuminuria and varying degrees of edema, the loss of body protein may amount to more than 25 Gm. a day. The chief principles of management of such patients include the restriction of salt according to the physiologic needs as estimated by determinations of the blood chloride concentration and the addition of extra protein to the diet. The question of fluid intake is debated, some maintaining that fluid intake should be restricted to 1,000 c.c. daily as long as marked edema is present, others stating that administration of pure water orally or dextrose solutions without salt slowly by vein will speed excretion of the salt and fluid retained in the tissues. The most reasonable view appears to be that when edema is present, salt intake should be restricted closely but rigid restriction of salt-free fluids is neither advisable

nor necessary, unless oliguria is present. Replacement of protein lost in the urine sometimes requires the prescription of a diet high in protein and supplemented with additional intermediate feedings of simple proteins or protein hydrolysates. The sodium chloride content of such preparations must be ascertained before use and the additional intake from this source recognized.

Drugs are of little value in the management of nephritis. Diuretics may be actually dangerous in their effect upon a damaged kidney, particularly if hematuria is present. Such drugs, especially mercurials, are neither indicated nor permissible in the treatment of renal edema.

**Uremia.**—Uremia may occur before operation as a result of a surgical disease in individuals with a low renal reserve, but this condition is much more frequently seen in such patients after operation. The uremic state probably develops in a patient with damaged kidneys following a rapid decrease in the circulating blood volume, which may result from loss of fluid through dehydration or vomiting, through the occurrence of postoperative shock, or through both. Decrease in the circulating blood volume or decrease in pressure in the renal circulation is responsible for a decrease in blood flow through the kidneys, with a resulting retention of urinary constituents in the blood. Uremia should be anticipated if the total urinary output drops to a low figure, especially if the specific gravity of the urine is low, and if the patient complains of headache, nausea, or drowsiness. Occurrence of these symptoms, and particularly the occurrence of a marked decrease in urinary output, necessitates the immediate determination of the urea or nonprotein nitrogen concentration of the blood. Measures for the treatment of uremia, however, should be instituted without delay as soon as the condition is suspected, blood chemistry studies being chiefly of confirmatory value. The patient's breath does not usually exhibit a uremic odor until the condition is well advanced.

Treatment consists of the slow administration of large quantities of fluid intravenously, either in divided doses of 1 liter each or by continuous infusion, until the daily urinary output reaches a total of 1,000 to 1,500 cubic centimeters. The fluid most suitable for intravenous use in these patients is dextrose (5 per cent) in distilled water. Normal salt solution is given only when blood chemistry studies show a deficiency in plasma chloride.

Although in the treatment of uremia sufficient fluid should be supplied to enable the kidneys to excrete the retained nitrogenous end products, so much should not be administered that the circulatory apparatus becomes overloaded, especially in patients with cardiovascular disease of any type. During administration of the fluid an attendant must remain with the patient to watch for such signs of cardiac strain as the appearance of slight dyspnea, moist râles, or venous congestion. At the first evidence of circulatory overloading the infusion must be discontinued. Rapid improvement in circulatory efficiency and therefore in renal blood flow sometimes may be secured in uremic patients by the slow intravenous administration of 25 to 50 per cent dextrose in doses of 50 to 100 cubic centimeters. Other measures occasionally successful in overcoming anuria include the use of medical diathermy applied over the kidney areas for twenty to thirty minutes, splanchnic block with procaine, and renal decapsulation. Decapsulation<sup>14</sup> of one or both kidneys in treatment of nonobstructive anuria is based upon the theory that spasm of the intrarenal vessels has occurred as a result of irritation or stimulation of the sympathetic nerves supplying the kidney and that decapsulation will effect removal of the renal sympathetic fibers with consequent release of vascular spasm. If the operation is to be undertaken, it should not be done until after nonoperative measures have proved unsuccessful following a thorough trial. To be of value, however, decapsulation should not be deferred for more than three or four days after the onset of pronounced oliguria.

### Diabetes

The incidence of diabetes is increasing concomitantly with the increase in life span of the general population. Various insurance statisticians have estimated that over 1 per cent of the total population of the United States, or more than 1,000,000 people, have diabetes, whether the disease is clinically recognized or not. Furthermore, as the life expectancy of the average individual increases, a greater number of diabetic individuals enter the age group in which surgical conditions are more likely to occur and, as a consequence, more and more are entering hospitals as surgical patients. Since the introduction of insulin relatively few diabetic patients die primarily from their metabolic

disease; most of them succumb to some associated complication, which is often surgical in nature. The necessity for a routine careful urinalysis on each new patient entering the hospital is obvious in view of the fact that over one-third of all individuals with diabetes require surgery for some condition during their lives.

In the preparation and aftercare of the diabetic surgical patient the close association of surgeon and internist is necessary to a degree far beyond that required by any other complicating disease. The surgeon, of course, is the one who bears the chief responsibility, but alone he is no more able to supply adequate and proper care of the metabolic disease than he is able to perform his operation unassisted. Although the surgeon, to realize the internist's indispensability, should know the principles of dietetic and insulin therapy, he usually has neither the time nor the detailed training requisite for management of a sick diabetic patient in whom insulin reaction, dehydration, vomiting, and coma may succeed each other with confusing rapidity. Management of this medical complication requires close cooperation with the laboratory and, since the presence of diabetes increases the operative risk considerably, the medical care of the patient is fully as time consuming and as necessary as the surgical treatment. Joslin<sup>16</sup> has said that since the surgical diabetic patient is six times as likely to die as the medical diabetic patient, he needs six times the attention.

It is not necessarily true that the well-controlled diabetic patient is a normal surgical risk. Because of the metabolic disease the diabetic patient is likely to develop generalized arteriosclerosis and sclerosis of the coronary arteries at an earlier age than the nondiabetic subject. The possibility of cardiovascular complications both before and after operation therefore must be added to the other hazards of surgery in such patients. The fact that coincidental diabetes does not raise the general surgical mortality more than it does can be attributed entirely to the increased and unremitting care that these patients usually receive.

Preparation, particularly in the elective case, is directed chiefly toward restoration of normal metabolism and storage of glycogen as protection against the anesthetic and its aftereffects. Careful search must be made for all possible foci of infection, such as dental abscesses, infected tonsils or sinuses, chronic or

acute respiratory tract disease, and cutaneous inflammations. These conditions, if present, should be corrected as far as possible, for their existence makes metabolic control of the diabetes more difficult. The question frequently arises as to whether attempts should be made to render the urine sugar free and to keep the blood sugar within normal limits. The general opinion at present seems to be that in children and young adults normal levels should be sought; in the middle-aged and especially in the aged the blood sugar should be kept slightly above normal. In the older age group a trace of sugar in the urine is not undesirable.

**ELECTIVE CASES.**—The life of the patient and the smoothness of his postoperative course depend in large part upon the glycogen reserve in the liver; maintenance and fortification of this reserve up to the time of operation are therefore major concerns. These objectives may be accomplished in the average case by administration of a diet relatively high in carbohydrate, high or at least adequate in protein, and low in fat for several days before surgery is undertaken, with control of the blood sugar level and promotion of normal carbohydrate metabolism and hepatic function by means of appropriate insulin dosage. For example an adequate diet might be one containing protein and fat in the ratio of 1 Gm. per day for each kilogram of body weight, with a total daily intake of carbohydrate amounting to 250 Gm. or more, according to the caloric requirement. The attending nurse should note whether the patient eats the entire meal in order to make sure that the preprandial dose of insulin is not excessive. Fluids, of course, should be taken in large amounts. The administration of vitamins is often advisable in a diabetic patient whose diet has been closely controlled for a long period.

Before operation is undertaken, the blood sugar should be stabilized within a range of 120 to 180 mg. per cent and the carbon-dioxide combining power should be not below 50 volumes per cent. Blood chemistry studies should be made daily until the sugar and the alkali reserve have reached a constant satisfactory level. The urine should be free of sugar or should contain only a trace, with no ketone bodies present. Most accurate control of the metabolic variations can be attained by keeping a close watch upon the fluctuations in blood and urinary sugar

in the absence of ketone bodies, indicates the blood sugar to be within the range of safety. A sugar-free urine, however, gives no information, even if the patient is actually on the verge of unsuspected insulin shock.

**LOCALIZED INFECTIONS.**—Such localized infections as carbuncles and cellulitis present a different problem. Surgery in such conditions is as imperative as metabolic control unless the patient is in coma. Rapid spread of infection and a higher mortality rate are much more likely to occur if surgery is postponed for several days until the blood sugar has been standardized and chemotherapeutic control vainly attempted. The focus of infection should be incised and drained as soon as evidence of localization is present, whereupon the diabetes will respond more readily to attempts at regulation. If control is still difficult, search will often reveal the presence of another infectious process.

Ketone bodies present in the urine under such circumstances may indicate acidosis resulting from the infectious process rather than from the diabetes. It is usually safe to delay anesthesia and operation for several hours until the patient's condition has been ascertained by determinations of blood sugar, carbon-dioxide combining power, chlorides, and nonprotein nitrogen and by examination of the urine. An attempt is made before operation to control acidosis by administration of insulin and fluids, preferably normal salt solution, as required. Too much time, however, should not be allowed to pass before the infection is surgically drained, since active infection interferes with metabolic regulation in the diabetic patient. The effectiveness of insulin, moreover, is decreased 50 to 75 per cent by the presence of a severe infection.

Chemotherapeutic and antibiotic agents are of the greatest value in management of pyogenic infections. Minor or even moderately severe local infections often can be controlled completely by systemic administration of the proper drugs in the dosage indicated. Use of drugs alone for treatment of pyogenic infections is a dangerous practice, however, if the patient has diabetes and particularly if the infection is located in an extremity. Subclinical circulatory deficiencies on an arteriosclerotic basis not uncommonly are present at a relatively early age. Prompt

drainage of pus therefore is imperative as soon as liquefaction has occurred to prevent development of spreading gangrene and generalized sepsis. Furthermore, the inflammation and toxicity characteristically caused by pyogenic infections are likely to precipitate metabolic disturbances in a patient who has even mild diabetes. For these reasons it may be dangerous to delay drainage of an infection after localization has occurred in the hope that vigorous chemotherapy will render operation unnecessary. The greatest value of sulfonamide and antibiotic drugs in these patients is their efficacy in preventing extension of the infection to the blood stream or to other body tissues. Sepsis and metastatic infection have always been responsible for the highest percentage of deaths in diabetic patients who succumb in the course of pyogenic infections. Prompt, adequate, and well-planned surgery must be combined with skillful treatment of the disturbed metabolism and with properly chosen chemotherapy in the management of pyogenic infections in the diabetic patient; none of the three aspects of treatment can be omitted with safety.

**HYPERTHYROIDISM.**—This condition affects the individual with diabetes in somewhat the same manner as infection. Carbohydrate metabolism will frequently be difficult to control in the presence of thyrotoxicosis. With improvement in hyperthyroidism and reduction of general metabolic activity the diabetes usually becomes more amenable to insulin management.

**EMERGENCY OPERATIONS.**—Conditions which threaten the life of the patient must be corrected at once with as little time as possible lost in control of the associated diabetes. Occasionally there may be no time to determine the blood sugar and alkali reserve, although a sample of blood should be taken and the indicated determinations made and recorded as soon as possible. If the urine, which always must be examined, contains sugar or ketones, measures should be taken to forestall the development of coma, although slight glycosuria and minimal acidosis are not contraindications to emergency operation.

Diagnosis of unrelated surgical disease in a diabetic patient is sometimes complicated by the fact that the onset of coma, although usually gradual, may be fairly abrupt and may in itself



produce a picture strongly resembling that of a surgical abdominal disease. Severe acidosis at times may produce nausea and vomiting, obstipation, and abdominal pain and tenderness, together with fever, tachycardia, and leucocytosis, before the onset of coma.<sup>17</sup> Glycosuria and ketonuria are sometimes present in marked degree as a result of unregulated diabetes alone, but comparable findings may also be present in an acute surgical emergency with similar onset. Diagnosis may be established by determination of blood sugar and alkali reserve levels while the usual emergency treatments for diabetic coma are being carried out. These measures produce an immediate improvement in the nonsurgical diabetic patient, which renders the diagnosis obvious, and they also serve as valuable preoperative preparation for a patient with a true acute abdominal lesion.

**Acidosis and Coma.**—Patients with moderate to severe acidosis without coma respond promptly to administration of from 25 to 50 units of regular insulin repeated at intervals of one-half to one hour until the condition is normal clinically and laboratory examinations of blood and urine show approximately normal findings. Relief of acidosis is expedited by administration of at least 1,000 c.c. of normal salt solution intravenously with or without small amounts of dextrose added. After a satisfactory response has developed following the second or third dose of insulin, subsequent doses may be reduced to 25 units or less as indicated and the patient may be given carbohydrate in the form of orange juice (200 c.c.) to accompany the insulin injection. Unless the patient is in or approaching coma, it is best not to administer over 50 units of insulin for the initial dose, since individuals with diabetes vary greatly in their response to insulin.

Patients who are admitted in *actual coma* require prompt treatment and close watching. Urine and blood examinations are begun and a dose of 50 to 100 units of insulin is given immediately, along with an intravenous infusion of 1,000 c.c. of normal salt solution. Well-wrapped hot water bottles and blankets are applied and an enema is given. Gastric lavage with warm sodium bicarbonate (1 per cent) solution is always indicated in the treatment of severe diabetic acidosis or coma and should never be

omitted. Another dose of 50 to 100 units of insulin is given one-half hour after the first, and another specimen of urine is obtained. According to personal preferences, an infusion of 5 per cent dextrose (300 to 500 c.c.) may or may not be given at this time. Subsequent doses of insulin, usually amounting to 25 to 50 units of insulin at intervals of one-half to one hour, may be accompanied by infusions of 5 per cent dextrose in normal salt solution (300 to 500 c.c.) every hour or every two hours. These infusions must be given slowly so that the sugar will not be lost in the urine. Oral administration of sugar in the form of orange juice (150 to 250 c.c.) is just as satisfactory if the patient has recovered sufficiently to take it. Examinations of the urine are made each hour or, at most, every two hours, even if catheterization is necessary, until the patient shows complete clinical recovery. The presence and persistence of urinary ketones, which indicate acidosis, are of much more significance than the presence of sugar, which may have been excreted following an infusion.

There is considerable disagreement among various authorities concerning the use of carbohydrate in treatment of diabetic coma, although of course all agree on the use of other supportive measures. One viewpoint is that insulin should be used without glucose<sup>19,20</sup> until after the coma has been controlled because glucose neutralizes insulin and also because the blood sugar is high during severe diabetic acidosis. Opponents to this point of view maintain<sup>20</sup> that such patients have lost a good deal of sugar in the urine since the onset of severe acidosis and coma and that the sugar as well as the other elements, together with insulin, should be replaced to permit return of normal carbohydrate metabolism. There is little difference in mortality rate statistics reported by proponents of the opposing views; it is probable therefore that the administration of small amounts of carbohydrate with the relatively large doses of insulin used in treatment of severe diabetic acidosis and coma will do no harm and will act as a factor of safety when used by physicians who care for such patients only occasionally.

Diabetes in children is much more difficult to manage, since insulin tolerance is so variable in the young. Usually the insulin requirement is relatively high, but it is frequently influenced by injuries and by the infections, such as coryza or oral sepsis, which

are so common in children. Subsidence of any infection that may be present will cause a sudden decrease in the insulin requirement; this effect must be kept in mind or unsuspected hypoglycemia may supervene.

Incipient shock or dehydration, which may result from the surgical disease, may be treated effectively in the presence of diabetes by means of an infusion containing 400 c.c. of 10 per cent dextrose, given intravenously together with 20 to 30 units of insulin. Any other procedures necessary for the treatment of the surgical shock can be carried out without regard for the diabetes. There is often no opportunity in a condition requiring immediate surgical treatment to build up the glycogen reserve nor should this be attempted too rapidly by the administration of massive doses of dextrose, which may simply be excreted in the urine. Administration of carbohydrate in amounts greater than 50 Gm. at one time is not indicated as preoperative preparation, even though the urine may contain little sugar, and in the presence of glycosuria intravenous administration of normal salt solution alone is preferable. In either case so much insulin should not be given that there might possibly be danger of the development of hypoglycemic shock during the course of the operation.

**Anesthesia.**—If the status of the diabetes is known, almost any diabetic patient can be given an anesthetic with safety. Ether, while the safest anesthetic from every other standpoint, is probably the most likely to produce or aggravate acidosis as well as to cause prolonged postoperative nausea and vomiting, and therefore its use is contraindicated. Acidosis which is present before operation, however, will be increased by any general anesthetic. Choice of anesthesia, in a properly prepared and well-regulated individual with diabetes, can be made to suit the operation involved if the anesthetist is skillful and if adequate postoperative care is provided. The gaseous anesthetic agents, especially the type with which a high concentration of oxygen is used (such as cyclopropane), are the most satisfactory general anesthetics if the metabolic control is not perfect, while ethylene or sodium pentothal may be used for operations of short duration even in the presence of mild acidosis. As a general rule, and particularly for those in whom the diabetes is not well controlled, local or spinal anesthesia is preferable. Avertin is definitely

contraindicated because of its potential toxic effect upon the liver. Operation is usually safe if the blood sugar is within a maximum range of 200 to 250 mg., but complications are likely to ensue if the carbon-dioxide combining power is as low as 40 volumes per cent<sup>21</sup> or less.

**After Operation.**—Regulation of carbohydrate intake and insulin dosage must be balanced to prevent the diabetic patient from developing either acidosis or insulin shock. Frequent and regularly timed urine specimens must be examined, especially for ketones, even if it is necessary to catheterize the patient during the first day. A specimen must always be obtained within eight hours after operation. For the first two days, specimens of urine should be examined every four hours, following which the usual diabetic routine collection may be resumed. A mild diabetes controlled by diet before operation may require small doses of insulin in the early postoperative period. If the patient is not vomiting, it is safe to allow oatmeal gruel, ginger ale, or other fluids on the surgical liquid diet list as desired for the first twenty-four hours after operation.

Adequate fluid intake must be assured; usually 2,500 to 3,000 c.c. will suffice to keep the urinary output at or above 1,000 c.c. daily. If necessary, most of this can be administered intravenously, either as 5 per cent dextrose in distilled water or as normal salt solution, although not more than 1,000 c.c. of the latter should be given in each twenty-four hour period without special indications. The carbohydrate intake should be maintained at approximately the normal level of 100 to 200 Gm. a day. If the patient cannot retain food by mouth, the required carbohydrate can be given intravenously as 5 per cent dextrose in several divided doses, with the required apportionment of insulin administered hypodermically or by addition to the infusion. Infusions of dextrose should be given very slowly to the diabetic patient to prevent loss in the urine. Absorption of sugar from the rectum is very slight and rectal administration therefore is not advised. Sufficient insulin to cover the amount of sugar used is given with each infusion, but consideration must be given to the facts that a moderate degree of glycosuria is usual after operations and that the insulin requirement decreases rapidly after the acute postoperative period is past. Hypoglycemic shock is frequent after this time if the dosage of insulin is not altered to meet the

circumstances; this form of shock must never be confused with postoperative shock, which it may strongly resemble.

If there is any doubt or uncertainty concerning the amount of insulin required, it is always preferable to give too little rather than too much and to repeat the doses as indicated. Symptoms of insulin overdosage and hypoglycemia occasionally take strange forms; if a patient's reactions or symptoms are puzzling, the administration of a small amount of orange juice by mouth or dextrose by vein may prove promptly effective.

With regard to insulin apportionment during the twenty-four hours of the operative day, *Joslin*<sup>16</sup> recommends administration of the daily total number of units regularly used by the patient but divided into small frequent doses every three hours, without relation to meals. If the patient has not been using insulin, it should be given when two successive urine specimens show the presence of sugar and omitted when two successive specimens are sugar free. Other alterations in the insulin dosage may be made on the basis of quantitative sugar determinations in the frequent urinalyses. For a rough approximation, the average patient may be given insulin according to Benedict's urinary sugar test as follows: green color, 5 units; yellow, 10 units; orange, 15 units; brick-red precipitation with decolorization of solution, 20 units. If more than 5 units is required, a quantitative sugar determination should be made. Some authorities employ protamine zinc insulin in a basic dose each morning before breakfast, with supplementary small doses of regular insulin once or twice a day for more accurate control of metabolic fluctuations.

As soon as the patient is able to retain food, a four-hour feeding schedule should be instituted, each feeding containing about 25 to 50 Gm. of carbohydrate and consisting of liquids and semisolids such as orange juice, ice cream, oatmeal, milk toast, and orange albumin, with the requisite sugar added. A normal feeding schedule should be resumed as soon as possible and can generally be attained within a week.

In other respects the surgical diabetic patient is treated in the same way as any other surgical patient. Wound healing and postoperative recovery should be normally rapid and uncomplicated if the diabetes is well controlled.

## References

1. Lahey, F. H., and Hurxthal, L. M.: Postoperative End-Results in 300 Thyrocardiacs, *Am. J. Surg.* 21: 225, 1934.
2. Marvin, H. M.: Heart During Anesthesia and Operative Procedures, *New England J. Med.* 199: 547, 1928.
3. Hamilton, B. S.: Chronic Cardiac as Surgical Risk, *S. Clin. N. America* 6: 621, 1926.
4. Butler, S., Feeney, N., and Levine, S. A.: The Patient With Heart Disease as a Surgical Risk; Review of 414 Cases, *J. A. M. A.* 95: 85, 1930.
5. Morgan, P. W.: Management of Paroxysmal Tachycardia Including Use of Mecholyl, *Ann. Int. Med.* 19: 780, 1943.
6. Herrmann, G., and Herrmann, L. G.: Cardiac Disorders in Surgical Patients; Criteria Used in Estimating Risk Involved, *Texas State J. Med.* 30: 183, 1934.
7. Harrison, T. R.: Abuse of Rest as Therapeutic Measure for Patients With Cardiovascular Disease, *J. A. M. A.* 125: 1075, 1944.
8. Levine, S. A.: Some Harmful Effects of Recumbency in Treatment of Heart Disease, *J. A. M. A.* 126: 80, 1944.
9. Wheeler, E. O., Bridges, W. C., and White, P. D.: Diet Low in Salt (Sodium) in Congestive Heart Failure, *J. A. M. A.* 133: 16, 1947.
10. Batterman, R. C., DeGraff, A. C., and McCormack, J. E.: The Effectiveness and Safety of Mercupurin Administered Orally, *J. A. M. A.* 124: 1243, 1944.
11. Brams, W. A., Golden, J. S., Sanders, A., and Koplan, I.: Observations on Toxicity and Clinical Value of Strophanthin, *Ann. Int. Med.* 13: 618, 1939.
12. Brumm, H. J., and Willis, F. A.: Surgical Risk in Patients With Coronary Disease, *J. A. M. A.* 112: 2377, 1939.
13. Fishberg, A. M.: Hypertension and Nephritis, ed. 4, Philadelphia, 1939, Lea & Febiger.
14. Van Slyke, D. D., Page, I. H., Hills, A., and Kirk, E.: Studies of Urea Excretion: Comparison of Urea Clearances Calculated From Excretion of Urea, of Urea Plus Ammonia, and of Nitrogen Determinable by Hypobromite, *J. Clin. Investigation* 11: 901, 1935.
15. Abeshouse, B. S.: Renal Decapsulation: Review of Literature and Report of 10 Cases, *J. Urol.* 53: 27, 1945.
16. Joslin, E. P.: Diabetic Surgery From Medical Point of View, Boston M. & S. J. 196: 127, 1927.
17. DeTakats, G.: Surgery in Diabetes, *J. Kansas M. Soc.* 36: 177, 1935.
18. Joslin, E. P.: Medical Progress; Diabetes Mellitus, *New England J. Med.* 232: 219, 1945.

19. Root, H. F.: Use of Insulin and Abuse of Glucose in Treatment of Diabetic Coma, *J. A. M. A.* 127: 557, 1945.
20. Almy, T. P., Swift, K., and Tolstoi, E.: Treatment of Diabetic Acidosis and Diabetic Coma, *J. A. M. A.* 129: 863, 1945.
21. Standard, S., Brandaleone, H., and Ralli, E. P.: Surgical Results in Treated and Untreated Diabetic Patients; Analysis of Altered Prognosis in Comparative Group of 474 Clinic and Nonclinic Patients, *J. A. M. A.* 110: 627, 1938.

## CHAPTER 11

# CHEMOTHERAPEUTIC AND ANTIBIOTIC DRUGS

One of the greatest recent advances in medicine has been the development of chemotherapeutic and antibiotic agents for the control of bacterial infections. Although these drugs have been in use for such a short time, the terrifying mortality rates of many of the most lethal bacterial diseases have been cut to incredibly low figures. So effective are these drugs that as each new related compound has been introduced, it has been greeted almost as a positive cure for diseases formerly regarded as hopeless. The period of extreme enthusiasm has begun to pass recently as the limitations, contraindications, and toxic effects of each drug are established, but discovery of newer and similarly effective related compounds is still proceeding while the therapeutic applications of the original drugs continue to be extended.

Proper use of these compounds requires a thorough acquaintance with their effects on both the patient and the invading microorganisms. Different bacteria are more susceptible to one drug than to another; different modes of administration of each drug produce different therapeutic effects; and the various chemotherapeutic and antibiotic agents differ with respect to their toxic effects on the patient. A reliable knowledge of the early manifestations of toxicity and of the entire range of toxic reactions possible is a prerequisite to the use of any drug of this class for any purpose. It is scarcely a therapeutic triumph for the drug to conquer an infection and yet to destroy the patient.

The most useful of the chemotherapeutic agents are the sulfonamide drugs, which are synthetic compounds. The sulfonamides act as bacteriostatics, inhibiting the multiplication of susceptible microorganisms probably by interfering with the oxidative reactions involved in this process. As in any chemical reaction, various factors may cause interference with the therapeutic effects of these drugs. Certain chemical compounds in the tissues will inhibit action of the sulfonamides, and the presence of exudate, pus, or necrotic tissue will hinder access of the chemotherapeutic agents to the bacteria. Also, toxic effects may be



produced on the tissues of the body by the drug if given in full clinical dosage. Finally, the maximum effectiveness of chemotherapeutic drugs is relatively specific, within limits.

Antibiotics are antibacterial substances produced by or derived from living organisms. While these substances at present cannot be synthesized commercially, they can be extracted from cultures of the living organisms in large enough quantities to meet clinical needs. It has been recognized for many years that one organism may exert an antibiotic (antagonistic) or symbiotic (stimulating) effect upon another, but the principle of antibiosis was not put into extensive therapeutic use until the discovery and large-scale development of penicillin. Fleming in 1929 noted inhibition of growth of staphylococci on an agar plate culture following accidental contamination with a mold, and investigated the phenomenon. By 1932 he reported<sup>1</sup> the clinical use and therapeutic effectiveness of a *Penicillium notatum* culture filtrate applied locally to infected wounds, a well-timed clinical application of a chance discovery. Florey, who, with his co-workers, first isolated penicillin and demonstrated its powerful activity against certain bacteria, later worked on a plan for mass production of the antibiotic. Within a period of three years, enough pure penicillin was being produced to supply the needs of the Armed Forces, with almost incredibly good results in the treatment of infection and disease.

Other antibiotics in current use include streptomycin (p. 306) and tyrothricin (p. 483). Many related substances are being investigated, and it is probable that future discoveries in this field will far exceed those made in the past few years.

While chemotherapeutic and antibiotic drugs have a wide range of usefulness in every field of medicine, discussion will be restricted to their uses in surgical diseases and in complications of surgery, fields which, however, overlap those of other medical specialties in many instances.

### Sulfonamides

Although sulfanilamide and its allied derivatives are of the greatest therapeutic value in the control of certain bacterial infections, their mode of action still is not finally explained. Neither sulfanilamide nor any of its related derivatives has a direct bactericidal effect upon susceptible organisms in vitro.

The theory originally proposed held that the specific drug in proper concentration interferes with the metabolic processes of the infecting bacteria by combining with a substance involved in an enzyme reaction necessary for bacterial growth and multiplication. Evidence was cited<sup>2</sup> to indicate that this necessary substance is potentiated by combination with para-aminobenzoic acid, to which the sulfonamides act as competing antagonists. According to this view,<sup>3</sup> some bacteria are able to synthesize para-aminobenzoic acid; others are not able to do so but derive it from the tissues of the host, particularly necrotic tissue. Since sulfonamides and para-aminobenzoic acid are both able to combine with an unidentified substance necessary for bacterial metabolism, sulfonamides in proper concentration therefore should reduce the amount available for potentiation by combination with para-aminobenzoic acid and thus restrain bacterial growth and multiplication. Similarly, the presence of an excess of para-aminobenzoic acid will restrain the therapeutic activity of the sulfonamides.

However, this reaction cannot be said to be specific; many other compounds besides para aminobenzoic acid will interfere with sulfonamide effect. Certain proteins, peptones, amino acids (methionine), and similar products found in pus and in urine will act as sulfonamide inhibitors. The theory that sulfonamides restrain bacterial growth by interfering specifically with para-aminobenzoic acid metabolism therefore is not a sufficient explanation. It is probably true, however, that the bacteriostatic effect of these drugs is due to inhibition of the activity of certain enzymes. A second theory,<sup>4</sup> following considerable experimental study, proposes that sulfonamides inhibit cell division by interfering with a specific fraction of the total cellular oxidative processes. According to this view, the effect of sulfonamides on cellular respiration is not sufficient to destroy the organisms but is sufficient to prevent the increased oxidative activity characteristic of cellular multiplication.

Sulfonamides are most valuable in treatment of infections due to certain gram-positive and gram-negative cocci. The susceptibility of these organisms to chemotherapy varies according to the type of infection produced, the rapidity of invasion, and the vascularity of the area involved. Pus and necrotic tissue present in an acutely infected area interfere with sulfonamide effect

both by production of sulfonamide inhibitors and by prevention of access of the drug to the infecting organisms or to their immediate environment. Chronic inflammatory processes, characterized by local scarring and tissue necrosis, similarly afford protection to infecting organisms against sulfonamides, whether applied locally or brought through the blood stream. On the other hand, conditions are optimum for sulfonamide therapy in acute processes marked by rapid spread and active invasion. In such infections, vascularity is increased in proportion to the extent of bacterial invasion and the sulfonamides in the blood find ready access to the organisms in the tissues, unprotected by excess inhibitors. When the infection is not eradicated quickly, however, areas of local tissue necrosis may develop. Such a complication, marked by continuance of fever and leucocytosis in spite of chemotherapy, indicates that local surgical measures also might be necessary to drain and eliminate a walled-off focus beyond the ability of the sulfonamides to eradicate.

Sulfonamides therefore are of less value in treatment of well-localized infections or abscesses, in which surgical drainage is more effective, nor are they of much value in treatment of mixed infections, in which one or more of the organisms is resistant to the action of the drug.

Therapeutic doses of most of the absorbable sulfonamides when given orally are absorbed completely through the small intestine within two to three hours, at which time the resulting concentration of sulfonamide in the blood reaches its height. For maintenance of an optimum level of free sulfonamide in the blood, the drug is best given every four hours during the day and night in dosage proportionate to the level desired. Sulfonamides in the blood stream are carried to all parts of the body in proportion to the vascularity of the tissues. Inflamed tissues, in which the blood vessels are dilated, show a proportionately higher sulfonamide content both in the tissue fluid and in the exudate.

Sulfonamides absorbed into the blood stream are partly conjugated in the liver to an acetylated form, which is less soluble than the free form and is almost completely inactive therapeutically. The degree of acetylation varies with the different sulfonamides. Both the free and the acetylated forms are excreted through the kidneys, complete excretion usually occurring within forty-eight hours. Excretion of sulfonamides can be hastened by

forcing fluids and increasing the urinary output, while restriction of fluid intake or the presence of kidney damage will delay excretion.

Optimum effect of the sulfonamides depends upon maintenance of the proper therapeutic level of the free drug in the blood as well as upon the type of organism, character and extent of infection, and general resistance of the patient. It is not always possible to secure laboratory determination of sulfonamide levels, however, and dosage often must be regulated according to clinical response. As a rule, infections of moderate degree due to susceptible organisms can be controlled by maintenance of a free sulfonamide concentration of 5 to 10 mg. per cent in the blood, while more severe or extensive infections require concentrations up to 10 to 15 mg. per cent. The desired therapeutic level usually is not reached for a day or more after the initial dose is given, since both the body tissue fluids and the blood plasma must be saturated equally with the drug and since the rates of absorption, conjugation, and excretion vary with different individuals. After the desired level is reached, a balance between excretion and intake is achieved by regulating the dosage according to therapeutic effect, with laboratory determinations of the blood sulfonamide concentration as an added guide. The most satisfactory laboratory technique for accurate determination of sulfonamide concentration is the procedure reported by Bratton and Marshall,<sup>6</sup> while a simple test for approximate levels<sup>6</sup> has been suggested by LaRosa.

Sulfonamides will produce *toxic effects* in certain patients even when used in small doses; caution is always necessary during the course of therapy. Mild reactions such as slight nausea, dizziness, headache, malaise, and moderate depression are non-specific and do not necessitate complete withdrawal of the drug. More serious manifestations include skin rash, drug fever, jaundice, progressive neutropenia, and hemolytic anemia. These reactions are signs of dangerous toxicity and always require immediate discontinuance of all sulfonamide therapy, forcing of fluids orally and intravenously to hasten elimination of the drug, and specific measures to correct the damage as far as possible.

Agranulocytosis or marked neutropenia occurring during sulfonamide therapy demands immediate discontinuance of

the sulfonamide and administration of large quantities of fluid to hasten excretion of the drug. Penicillin is given to prevent the development of secondary infections. Such infections are the usual cause of death in patients with agranulocytosis, and if sepsis can be prevented until the damaged bone marrow again begins to produce leucocytes in normal numbers, recovery is likely. Large doses of penicillin (50,000 units intramuscularly every two hours) are advisable. Pentnucleotide may be given intragluteally in a dose of 10 c.c. four times daily until the leucocyte count begins to rise and then once or twice daily until the count is normal. Yellow bone marrow concentrate also may stimulate maturation of leucocytes and is given orally in doses determined by the marrow content of the preparation employed.

Hematuria, oliguria, and anuria are caused by precipitation of the relatively insoluble acetyl forms of the sulfonamides in the renal collecting tubules and in the kidney pelves and ureters; there is evidence also that a direct toxic effect on the renal epithelium is often a factor. In the latter case, the hemoglobiuric nephrosis closely resembles that occurring in association with hemolytic transfusion reaction or crush syndrome. While microscopic hematuria and the appearance of occasional crystals in the urine do not necessitate discontinuance of sulfonamide therapy, they do indicate the need for close watch for oliguria and for the presence of hematuria of more significant degree. Since the acetyl forms of the sulfonamides are more soluble in alkaline solution, it is customary to administer sodium bicarbonate along with each dose of the chemotherapeutic drug. Amounts of 1 to 2 Gm. are used, although alkalization of the urine usually requires a total of 15 to 20 Gm. of sodium bicarbonate daily. When oral administration is impossible or undesirable, sodium lactate solution (1, 6 molar) can be given intravenously<sup>7</sup> as an effective substitute in amounts of 500 to 1,000 c.c., repeated as necessary to alkalize the urine. One liter of this solution (containing 18.66 Gm. of sodium  $\gamma$ -lactate) will induce urinary alkalinity within several hours and maintain it for twenty-four hours.

Oliguria and hematuria appearing during sulfonamide therapy require immediate discontinuance of the drug, administration of fluids orally and dextrose (5 per cent) solution intravenously, and alkalization of the urine to at least pH 7.5 by

infusion of sodium lactate solution (1/6 molar). Bilateral catheterization of the ureters and irrigation of the kidney pelves should be done without further delay if anuria or oliguria has been present for as long as twenty-four hours and hematuria and crystalluria are present. If the suppression of urine is due to extrarenal precipitation of crystals, these procedures will suffice in most cases. When anuria is due to intrarenal damage, however, other measures are necessary. Diuretic solutions such as dextrose 10 per cent (1,000 c.c.) or dextrose 50 per cent (50 to 100 c.c.) can be given intravenously and diathermy can be applied to the kidney regions, although little can be expected from these methods of stimulation as a rule. Anuria is a serious complication; if it does not respond promptly to the measures already outlined, the only other treatment of value is renal decapsulation. Several authors have reported instances in which anuria following sulfonamide therapy has been relieved by prompt decapsulation of one or both kidneys<sup>3</sup> and agree in advising that the procedure be done without delay if conservative treatment fails. Decapsulation is only occasionally effective, at best.

While certain of these toxic effects are more characteristic of one drug than another, even the least toxic sulfonamide occasionally can produce a fatal reaction. Appearance of any one of the serious toxic manifestations during sulfonamide therapy signifies sensitivity to the drug. Further use of the same drug even at a much later date is likely to be followed by the same toxic response. Sensitivity to one sulfonamide drug does not necessarily indicate sensitivity to the entire group, although this does sometimes occur. Since sensitivity persists for years, it is a wise precaution before administering sulfonamides to inquire if the patient has taken a drug of this group at any time previously and if toxic reactions resulted at that time. Because of the possibility of sensitization, no patient should be given sulfonamides, especially in full dosage, for a minor condition.

**Sulfanilamide (Para-Aminobenzenesulfonamide).** — This drug, only a few years ago the mainstay of treatment for streptococcic infections, is now little used; other sulfonamide drugs of lower toxicity and equal or superior therapeutic effect have been developed. At present, the chief use for sulfanilamide is for local application to fresh wounds to prevent or delay in-

fection, although even this procedure has been almost generally abandoned.

Sulfanilamide is still used occasionally for treatment of infections due to hemolytic streptococci or meningococci if the patient is unable to take sulfadiazine. Sulfanilamide is of little value in other coccal infections or in infections due to the hemolytic streptococcus of Lancefield, groups B and C, or to anaerobic or nonhemolytic streptococci or to *Streptococcus viridans*. It is occasionally of some value in the management of urinary tract infections due to *Escherichia coli*.

If sulfanilamide is to be used, a moderately ill adult patient can be given 3 to 4 Gm. (gr. 45 to 60) as the initial dose and 1.0 Gm. (gr. 15) every four hours thereafter throughout the day and night for as long as necessary. This dosage ordinarily will be sufficient to produce and maintain a level of free sulfanilamide in the blood of at least 10 mg. per cent. Sodium bicarbonate is given in association with sulfanilamide in amounts of 2 Gm. with each dose to decrease the formation of the toxic acetylsulfanilamide. Effective concentration of the drug should be maintained for at least several days after all evidences of the infection have disappeared, particularly if localized abscesses or areas of necrosis are present.

Patients who are too ill to swallow the large doses required or who are vomiting may be given sulfanilamide by hypodermoclysis or by vein, although oral administration, following which absorption of the drug into the blood stream is slow and prolonged, is to be preferred whenever possible. Sulfanilamide is soluble in water in sufficient quantity to form an 0.8 per cent solution and may be given parenterally in sterile distilled water or in normal salt solution. One-half the total dose for the first day is administered in the initial hypodermoclysis or infusion and the treatment is repeated every eight hours, each dose after the first containing one-third the required daily total. Blood sulfanilamide determinations are made frequently and the dosage adjusted accordingly.

In less severely ill patients sulfanilamide is given by mouth in doses of 0.6 to 1.0 Gm. (gr. 10 to 15), with 1 to 2 Gm. of sodium bicarbonate, every four hours of the day and night to reach and maintain the desired blood level of 5 to 10 mg. per cent of the

drug. Full therapeutic doses are continued for several days after all evidence of infection has disappeared.

*Local use of sulfanilamide in wounds* for direct bacteriostatic effect was first begun shortly after introduction of the drug. Because sulfanilamide is relatively soluble in water and hence in body fluids, it was believed that the growth of locally contaminating bacteria in fresh wounds, burns, or areas of early peritonitis would be inhibited by the drug. Many clinical reports appeared, indicating that in a high percentage of cases wound infection or peritonitis was prevented by the local application of sulfonamides and that the period during which fresh traumatic wounds could be considered as contaminated rather than infected might be extended for many hours. Wide-spread use of the drug in this way may have led to carelessness in its application, to lack of appreciation of its limitations, or to relaxation in observance of fundamental surgical principles. Whatever the reasons, less satisfactory results following local application of sulfanilamide began to appear, and at the present time<sup>9</sup> use of sulfonamide powder or crystals directly in a wound or infected area is not considered to be of benefit. At the beginning of World War II a War Department directive was issued ordering the first-aid application of sulfanilamide crystals and a sterile dressing to any wound sustained in battle. By the end of the war in Europe, another order<sup>10</sup> was issued, cancelling the previous directive and stating that sulfonamides were not to be used locally in wounds.

A clinical study and appraisal of the value of sulfonamides, administered both locally and generally, was reported by Meleney and Whipple<sup>11</sup> in 1945. The report was based on the results obtained in nine medical centers throughout the United States by controlled treatment of wounds with and without chemotherapy. A statistical analysis of the results indicated definitely that the routine use of sulfonamides locally or systemically or both reduced neither the occurrence nor the severity of infections developing in fresh traumatic wounds but that the systemic use alone of sulfonamides reduced the likelihood of spread of the infection into the general circulation with septicemia. The report further stated that systemic administration of sulfonamides was as effective in preventing the spread of infection if not given until clinical evidence of infection developed as it was if given



prophylactically. However, if prophylactic systemic chemotherapy is not instituted in patients with open traumatic wounds, it is necessary to watch closely for the earliest signs of spreading infection.

There are several possible explanations for the disappointing lack of effect of sulfonamides applied locally. Wound exudates, dead bacteria, and necrotic tissue not only mechanically interfere with access of the sulfonamide to the living bacteria, but also contain substances which inhibit the action of the drug. Sulfanilamide, being relatively soluble, is absorbed fairly rapidly and an initial high local concentration of the drug is produced but soon drops below an effective level and disappears. Since the sulfonamides are bacteriostatic rather than bactericidal, the few remaining bacteria begin to proliferate and invade as soon as the sulfonamide concentration is reduced. The infection therefore is delayed but not prevented. If large quantities of sulfanilamide or smaller quantities of a less soluble drug such as sulfadiazine are used to obtain more prolonged effect, the undissolved portion forms a solid dry mass and acts as a foreign body. Finally, the use of a sulfonamide locally may perhaps be instituted to offset lack of appreciation or lack of employment of the sound basic principles of surgery with respect to proper débridement, proper dressing, and proper aftercare of the wound and of the injured patient.

Many surgeons still believe that, if correctly used, sulfonamides applied locally will reduce the incidence of wound infection. If these drugs are used in this way, the drug of choice is sulfanilamide, since the rate of absorption of the other sulfonamides is undependable and irregular. Furthermore, the sterile drug should be used in microcrystalline or powdered form and should be sprinkled in a thin frosting over the surface of the wound so lightly that the color of the tissue can be seen through it in all areas; a thick layer or heap of the drug is not to be desired. Applied in this way as a supplement to proper débridement of the wound, sulfanilamide is at least unlikely to cause harm. Local use of the drug for intraperitoneal or intrathoracic infection should follow the same method of light dusting rather than of pouring in a predetermined quantity (for example, 5 Gm.). Local application of powdered sulfanilamide in amounts of 5.0 Gm. was formerly widely used in the treatment of localized

peritonitis; for example, in acute appendicitis with perforation. In recent years, such local applications of sulfanilamide have been largely replaced by prophylactic or therapeutic administrations of sulfonamide or antibiotic drugs systemically, although some writers<sup>12</sup> still favor the use of sulfanilamide locally in intraperitoneal infections.

It is to be remembered that soluble sulfonamides applied to the surface of the wound and more especially to an extensive burn are absorbed rapidly and may produce an extremely high concentration of the drug in the blood. If these drugs are used locally on an open surface, they should be used in small quantities (not over 5.0 Gm.) to prevent overdosage by rapid absorption into the circulation.

*Toxic effects* of sulfanilamide are greater than those caused by more recently introduced related compounds. Patients who are receiving full therapeutic doses of sulfanilamide should be kept under supervision in the hospital throughout the course of treatment. Temperature readings are made and recorded every four hours, urine examinations are performed daily, and blood hemoglobin determinations and white blood cell counts are obtained at least every four days in order to detect the appearance of toxic manifestations in their earliest stages. Alcoholic liquors increase the potential toxicity of sulfanilamide and should not be used by a patient taking the drug.

The most commonly observed toxic effects include anorexia, nausea, vomiting, dizziness, headache, mental depression, and acidosis. In some cases a macular or maculopapular rash is produced, but the eruption usually is transitory in nature and leaves no permanent marks. Drug fever also may occur occasionally. The symptoms of general malaise and psychic depression often observed in the course of sulfanilamide therapy may be marked enough to be distressing to the patient and to require a change of therapy. It is worth noting that sulfonamides, particularly sulfanilamide, may cause slowing of reaction time and confusion of thought. No work should be done and no machine should be operated (especially an automobile) by an ambulatory patient while these drugs are being taken in therapeutic dosage and for several days thereafter.

More severe reactions of sulfanilamide poisoning depend on the effects of the drug upon the red blood cells and upon the hemo-

poietic system. Cyanosis is the commonest manifestation of this type and appears first in the nail beds and lips and later over the entire body; visible cyanosis develops when the amount of methemoglobin in the blood exceeds 5.0 Gm. per cent. As the severity of erythrocyte damage increases, hemoglobinuria may develop and must be regarded as a dangerous sign foreshadowing the appearance of acute hemolytic anemia, sometimes also with jaundice as a result of the widespread hemolysis. Since sulfanilamide exerts its toxic effect in susceptible patients on either or both types of marrow cells, agranulocytosis may result, with or without hemolysis. The drop in white blood cell count may occur gradually over a period of several days or may develop suddenly within a few hours; in some cases, granulocytopenia may not appear until after administration of sulfanilamide has been discontinued. Sulfanilamide and its allied compounds have been reported in isolated instances to cause hepatic damage of a type resembling acute yellow atrophy.

Management of toxic reactions to sulfanilamide therapy is directed chiefly toward their prevention. Sodium bicarbonate is given routinely in association with the drug to minimize the tendency to production of acidosis and formation of methemoglobin. Fluids are supplied in sufficient amounts to maintain a daily urinary output of 1,500 c.c., although this tends to reduce the concentration of the drug in the blood. The milder toxic manifestations (nausea, slight depression) are not sufficient reason for discontinuance of the drug but do require increased vigilance to detect any evidence of poisonous effects on the blood cells or bone marrow.

Severe nausea, vomiting, marked mental depression, skin rash, drug fever, and oliguria are all evidences of serious toxicity; any one of these manifestations indicates immediate discontinuance of the drug. Slight to moderate cyanosis is not an indication for withdrawing sulfanilamide, although the dosage should be decreased. Administration of the drug is stopped entirely if a fall in hemoglobin concentration or leucocyte count is observed or if hemoglobinuria or jaundice develops. Sulfanilamide is eliminated gradually, chiefly by the kidneys; elimination may be hastened by giving large quantities of fluids orally or intravenously to increase the urinary output. Transfusion of

blood is rarely necessary, although infusions of dextrose solution will encourage diuresis and support the liver, which may be damaged by overdoses of sulfanilamide.

**Sulfapyridine** (2-*p*-aminobenzenesulfonamido-pyridine).—This drug, the first chemotherapeutic agent effective in pneumococcic pneumonia, is no longer employed to any great extent. It is the most toxic of the sulfonamides in clinical use and for this reason has been replaced by newer drugs equal or superior therapeutically and much lower in toxicity.

**Sulfathiazole** (2-sulfanilamidothiazole). — Although less effective than penicillin, sulfathiazole is the best of the sulfonamides for treatment of staphylococcic and gonorrheal infections. It is of value in the treatment of urinary tract infections due to staphylococci but has less effect upon *Escherichia coli*, *Streptococcus fecalis*, and *Pseudomonas aeruginosa* (*Bacillus pyocyaneus*).

Sulfathiazole is second choice to sulfadiazine in the treatment of pneumonia or other infections due to the pneumococcus. It is not of much use in treatment of meningitis since it does not appear in the cerebrospinal fluid in as high a concentration as do the other sulfonamides. Sulfathiazole is no longer used so extensively since the introduction of sulfadiazine, which is equally effective, less toxic, and less likely to induce crystalluria. It is frequently used in combination with other sulfonamides (p. 292).

The drug is absorbed rapidly from the gastrointestinal tract and reaches maximum concentration in the blood and the body tissues within three to six hours after administration. Free sulfathiazole is excreted more rapidly through the kidneys than any of the other systemically acting sulfonamides, so that the desired therapeutic level of this drug is somewhat more difficult to maintain. Sulfathiazole is conjugated to the therapeutically inactive and relatively insoluble acetyl form to a lesser degree than sulfapyridine but to a higher degree than any of the other commonly used sulfonamides. While conjugation may be almost absent in some patients, as much as 30 per cent of the drug may be acetylated in others. Since acetylsulfathiazole is of low solubility, it may crystallize in the urinary tract upon excretion.

Concentrations of free sulfathiazole in the blood amounting to 5 to 10 mg. per cent are effective in the treatment of moderately severe staphylococcic infections and of pneumococcic pneumonia. Bacteremia or septicemia due to the staphylococcus may require levels of 10 to 15 mg. per cent of the free drug.

Sulfathiazole is of low solubility and is given only orally; for intravenous administration, sodium sulfathiazole is used as a 5 per cent solution in sterile distilled water. This form of the drug is excreted rapidly, however; it is difficult to maintain a satisfactory therapeutic level by intravenous administration. In treatment of infections due to the staphylococcus, adults are given an initial dose of 3 to 4 Gm. (gr. 45 to 60) of sulfathiazole orally, followed by 1.0 Gm. every four hours day and night until the patient's temperature has been normal for three days. Children are given an initial dose of 0.15 Gm. per kilogram of body weight, the dose not to exceed the adult dose, and the same amount is given thereafter as the total daily dosage; it is administered in equal fractions every four to six hours until the patient's temperature has been normal for thirty-six hours. The dosage is then reduced by half and is continued until clinical evidence of infection has disappeared. Sodium bicarbonate in double dosage is given with sulfathiazole.

When sulfathiazole is given for treatment of staphylococcic septicemia, prolonged administration of the drug is necessary. For this type of infection in adults, an initial dose of 4.0 Gm. of sulfathiazole is given, followed by 1.5 Gm. every four hours day and night until the temperature has been normal for two days. The dose is then reduced to 1.0 Gm. every four hours and administration is continued for fourteen more days. Children with severe staphylococcic infections are given an initial dose of 0.2 Gm. of sulfathiazole per kilogram of body weight, the dose not to exceed the adult dose, and the same amount is given thereafter as the total daily dose in equal fractions every four to six hours. Administration is continued until the temperature has been normal for forty-eight hours, when the dose is decreased by one-third and is continued for fourteen more days. Sulfathiazole must be administered over a long period of time in treating staphylococcic septicemia to prevent the occurrence of a relapse. During the period of therapy with the drug, the total

output of urine is measured and recorded each day, the urine is examined at frequent intervals, and white blood cell counts are made regularly. Surgical drainage of localized foci of infection is a necessary adjunct to drug therapy, since sulfonamides will not affect such inaccessible areas. Sulfathiazole should not be used in the treatment of minor staphylococcic infections, both because of its possible toxicity and to avoid sensitization.

Although powdered or microcrystalline sulfathiazole has been used locally in chemotherapy of wounds, it is not advised for this purpose. Sulfathiazole is too insoluble and too irregularly absorbed to be of value and may produce a foreign body reaction during the healing phase.

*Toxic effects* due to sulfathiazole resemble those produced by the other sulfonamide drugs but are generally less severe. Sulfathiazole causes less nausea, vomiting, headache, dizziness, malaise, and cyanosis than any of the other commonly used sulfonamides, and these symptoms rarely require discontinuance of the drug.

Of more serious import are the skin rashes<sup>13</sup> of various types and the drug fever which may develop during the course of therapy, usually between the fifth and ninth days. The delay in development of drug fever sometimes allows it to be confused with an extension or flare-up of the infection for which the patient is being treated. Leucopenia and hemolytic anemia, while somewhat uncommon, also have been observed. Conjunctivitis, sometimes of marked degree, occurs as a toxic effect, although this disturbance has not been noted to result from the administration of any of the other sulfonamide drugs. Occurrence of any of these more significant toxic effects indicates immediate withdrawal of the drug and administration of fluids in large quantities to eliminate the retained sulfathiazole rapidly.

Hematuria and oliguria, appearing several days after institution of sulfathiazole therapy, require immediate discontinuance of the drug. These symptoms are due to precipitation of acetylsulfathiazole crystals in the collecting tubules of the kidney and in the renal pelvis and ureter, although in some patients the drug appears also to exert a direct toxic effect on the renal epithelium. Prompt corrective measures are required and should be instituted without delay (p. 280).

**Sulfadiazine** (2-sulfanilamidopyrimidine).—This drug is less toxic than sulfathiazole and is so much less toxic than sulfanilamide and sulfapyridine that it has practically replaced the latter two compounds for systemic use. Sulfadiazine is effective in the treatment of infections due to the beta-hemolytic streptococcus, pneumococcus, staphylococcus, gonococcus, and meningococcus. It is of value also in acute urinary tract infections due to *Proteus vulgaris*, *Pseudomonas aeruginosa*, or *Aerobacter aerogenes*. Chronic urinary tract infections respond less well. This drug is frequently used systemically in prophylaxis against secondary infection following burns, severe traumatic wounds, or operations involving peritoneal contamination.

Sulfadiazine is absorbed rapidly and well from the gastrointestinal tract and is excreted slowly, so that a constant satisfactory therapeutic level in the blood is easily maintained. It is found also in relatively high concentration (50 per cent) in the cerebrospinal fluid. About 15 per cent of sulfadiazine is conjugated to the acetyl form in the liver and may be precipitated in the urine. Both sulfadiazine and acetylsulfadiazine are much more soluble in alkaline than in acid urine, so that proper alkalization of the urine during administration of the drug will tend to prevent precipitation of crystals in the urinary tract.

For treatment of susceptible infections in an adult patient, sulfadiazine is given in an initial dose of 3 to 4 Gm. (gr. 45 to 60), with a maintenance dose of 1.0 Gm. (gr. 15) every four hours day and night, together with sodium bicarbonate. Optimum level of the drug in the blood is from 10 to 15 mg. per 100 c.c.; above this, precipitation of crystals in the urine is likely to occur. If parenteral administration is necessary, sodium sulfadiazine may be given intravenously as a 5 per cent solution in distilled water, in an initial dose of 0.06 Gm. per kilogram of body weight, with a maximum single dose of 5.0 Gm. Administration by hypodermoclysis is also satisfactory, a 0.5 per cent solution of sodium sulfadiazine in normal salt solution being employed. Oral administration is begun as soon as possible; until then, sodium sulfadiazine is given parenterally every twelve hours in a maintenance dose of 0.05 Gm. per kilogram of body weight. Frequent determinations of the concentration of free sulfadiazine in the blood are advisable; levels between 5

and 10 mg. per cent are maintained. Alkalinization of the urine is effected with sodium *r*-lactate solution (1/6 molar) given intravenously<sup>7</sup> in doses of 500 to 1,000 cubic centimeters. Sodium sulfadiazine and sodium lactate are incompatible in solution; if the same infusion apparatus is used for administration of both drugs, it should be cleared with several hundred cubic centimeters of normal salt solution after one drug has been given and before the other is introduced. Dextrose solution also is unsatisfactory in direct combination with sodium sulfadiazine.

For children, sulfadiazine is at present the drug of choice when a sulfonamide is needed. It is given in a dosage based on weight, the initial dose amounting to 0.1 Gm. per kilogram of body weight, not to exceed the adult dose. The total daily maintenance dose is the same as the initial dose but is divided into equal fractions given at four- to six-hour intervals or, for parenteral use, into two fractions given at twelve-hour intervals. Children reluctant to take tablets by mouth will usually take one of the more palatable proprietary suspensions of microcrystalline sulfadiazine, which contain 0.32 to 0.5 Gm. (gr. 5 to 7½) of the drug to each teaspoonful.

Administration of sulfadiazine is continued until the temperature has been normal for forty-eight to seventy-two hours and is then either stopped or continued in diminishing dosage according to the type and severity of the infection.

*Toxic effects* of sulfadiazine usually are mild. The occurrence of crystals in the urine during administration of sulfadiazine is common and does not in itself indicate necessity for reduction of dosage or withdrawal of the drug. The pH of the urine should be tested and enough alkali given to maintain an alkalinity of pH 7.5 or more, with a total daily urinary output of 1,500 c.c., since both sulfadiazine and acetylsulfadiazine are much more soluble in alkaline urine. Microscopic hematuria necessitates the reduction of dosage. Gross hematuria and oliguria are the two danger signals in patients receiving either sulfadiazine or sulfathiazole. These manifestations require prompt abandonment of the drug, administration of alkalies, and forcing of fluids. Acute hemolytic anemia, drug fever, and toxic dermatitis, although of extreme rarity in sulfadiazine therapy, may occur and require prompt measures similar to those given before. Complete anuria occurring during sulfadiazine therapy is treated according to the methods already outlined (p. 281).



Recent reports indicate that combinations of sulfadiazine and sulfathiazole administered simultaneously in half-dosage of each will prove equally as effective clinically as either drug alone in full dosage and will be less likely to be accompanied by renal complications<sup>14</sup> such as hematuria and oliguria. Decreased concentration of each drug decreases the degree of conjugation (acetylation), moreover, the presence of one acetylated sulfonamide in the urine does not decrease the solubility of the other. An additional advantage of the lowered degree of acetylation therefore is that alkalization of the urine is not necessary<sup>15</sup> when the sulfonamides are given in half-dosage in combination. A triple combination of sulfathiazole, sulfadiazine, and sulfamerazine in one-third dosage of each is also effective therapeutically and perhaps even safer from the standpoint of diminished incidence of crystalluria. Although alkalis can be omitted safely when average therapeutic doses of "triple sulfonamides" are taken, a high fluid intake should be maintained. The daily urinary output should average 1,500 c.c. and the urine should be examined at frequent intervals.

**Sulfamerazine (Sulfamethyldiazine).**—This drug resembles sulfadiazine in its effects, actions, and indications. It is absorbed more rapidly and excreted more slowly than sulfadiazine, so that less is required to produce effective therapeutic levels of the drug in the blood, and doses may be given at longer intervals.

For severe infections due to the pneumococcus or to the streptococcus, an initial oral dose of 3 to 4 Gm. of sulfamerazine is given, followed by a maintenance dose of 1.0 Gm. every eight to twelve hours. The optimum blood sulfamerazine concentration of 10 to 15 mg. per 100 c.c. is reached several hours after administration of the initial dose, and the interval between maintenance doses is regulated by occasional determinations of the concentration of the free drug in the blood. In children, the initial dose may vary from 0.5 to 1.5 Gm., followed by a maintenance dose of 0.25 to 0.75 Gm., depending upon the patient's size and age, administered every twelve hours. If intravenous administration is required, the same initial dose is given in the form of a 1.0 per cent solution of sodium sulfamerazine in sterile distilled water, followed either by routine oral administration or by repeated intravenous administration of the

maintenance dose every eight to twelve hours. Oral administration is preferred; the drug is given by vein only when necessary.

Both free sulfamerazine and acetylsulfamerazine are more soluble in urine than the corresponding forms of sulfadiazine. While crystalluria and renal precipitation are less likely to occur with sulfamerazine than with sulfadiazine, it is still advisable to administer sodium bicarbonate daily in sufficient dosage to maintain urinary alkalinity and decrease the likelihood of drug precipitation. If a combination of sulfonamides is used, alkalinization of the urine is unnecessary (p. 292)

Sulfamerazine is of about the same degree of toxicity as sulfadiazine. Because smaller doses of sulfamerazine are required and because it is less likely to cause precipitation of crystals in the kidneys or in the urine, it may prove to be somewhat more advantageous than other sulfonamides. The usual precautions are necessary: maintenance of an accurate fluid intake and output chart, determinations of the concentration of the drug in the blood, estimation of the hemoglobin concentration and white cell count every four days, routine and repeated examination of the urine, and observation of the temperature chart. The only serious complications so far reported following use of sulfamerazine are those due to precipitation of crystals in the urinary tract.

### INTESTINAL ANTISEPSIS

Certain sulfonamides, when administered orally, are poorly absorbed from the intestinal tract. The high concentrations of these drugs that can be developed within the lumen of the bowel have made intestinal bacteriostasis, if not intestinal antiseptis, possible. Sulfonamides of this group are used for treatment of certain bacterial infections of the intestinal tract and for reduction of the bacterial flora of the colon prior to surgery on this area.

**Sulfaguanidine (Sulfanilylguanidine).**—This drug, the first sulfonamide introduced specifically for intestinal bacteriostasis, is no longer widely used. Although it is relatively nontoxic, absorption from the intestinal tract occurs in sufficient quantity to require limitation of dosage. The usual dose given for preoperative intestinal antiseptis amounts to 0.1 Gm. per kilogram of body weight initially, followed by a maintenance dose of 0.05

Gm. per kilogram of body weight every eight hours for seven days before operation, and, if possible, for at least several days after operation. Concentration of sulfaguanidine in the blood may rise to 4 mg. per cent on this dosage. Although toxicity is not great, mild reactions may occur, and repeated white cell counts are advisable during sulfaguanidine therapy to detect a possible leucopenia. A very satisfactory reduction in bacterial count of the colonic contents results, and sulfaguanidine is useful if none of the later drugs of this class is available.

**Sulfasuxidine (Succinylsulfathiazole).**—This drug is absorbed from the bowel in extremely small amounts, only about 5 per cent or less being eliminated through the kidneys. Although the concentration of sulfasuxidine in the bowel may be elevated to an extremely high level, the level of the drug in the blood is usually below 2.0 mg. per cent. It is therefore of value only for intestinal antiseptics. Sulfasuxidine is particularly effective against the colon bacillus and the dysentery bacillus but exerts less inhibitory effect on typhoid and paratyphoid bacilli, *Streptococcus fecalis*, and *Proteus vulgaris*.

Poth and Knotts,<sup>14</sup> reporting on the use of succinylsulfathiazole, state that coliform organisms in feces normally number from 1,000,000 to 100,000,000 per gram of wet feces and that the gram-positive organisms are present in an equal number. Effective doses of sulfasuxidine will reduce the *Escherichia coli* count almost to zero and the other organisms to perhaps one-millionth of their original numbers within a week.

The preoperative preparation recommended by Poth<sup>15</sup> includes a low residue diet, avoidance of enemas or cathartics, and administration of succinylsulfathiazole in a dosage of 0.5 Gm. per kilogram of body weight during the first day and 0.25 Gm. per kilogram each day thereafter, each day's dose to be divided into six fractions and given orally at four-hour intervals, or, more simply, as 3.0 Gm. every four hours. Within three days, the stools begin to alter and within less than a week the patient's abdomen is flat and the stools are small, soft, odorless, free from gas, and low in bacterial content. The presence of diarrhea or the use of mineral oil will interfere with the concentration and effect of sulfasuxidine in the colon.

Operation on the bowel after this type of preparation even with the omission of enemas is much less likely to be followed by infection<sup>15</sup> of the peritoneal cavity or of the incision. Following operation, the same maintenance dose of sulfasuxidine is continued for a week, beginning as soon as the patient is able to swallow the drug.

Because of the small percentage of the drug absorbed into the circulation, toxic reactions are uncommon and are usually mild. Rarely agranulocytosis may occur in a patient who has been sensitized to sulfathiazole or succinylsulfathiazole by previous courses of treatment or by large doses of the drug over a long period. Routine frequent observations of the leucocyte count therefore are indicated during administration of sulfasuxidine.

**Sulfathalidine (Phthylsulfathiazole).**—This drug was introduced by Poth and Ross in 1943, and has been tested and used widely<sup>16</sup> in the same manner as its predecessor, sulfasuxidine. Each drug has individual advantages. Sulfathalidine is absorbed into the blood stream to even less extent than sulfasuxidine, the concentration of the drug in the blood usually varying between 0.5 and 1.5 mg. per cent, even after prolonged administration. It has approximately twice the bacteriostatic effect of the earlier drug, so that much smaller doses are required for preoperative preparation for colonic surgery or for treatment of susceptible intestinal infections. The chief disadvantage of sulfathalidine in preparation for bowel surgery is that the stools are solid and occasionally even hard following its use. Since enemas and irrigations are not advisable in combination with intestinal bacteriostatics, sulfasuxidine is perhaps preferable for preoperative use because it reduces the bulk and consistency of the stool as well as the bacterial count. In the presence of diarrhea or when cathartics or enemas may be used, however, sulfathalidine is more effective than sulfasuxidine. Both drugs are of some value in the treatment of chronic bacterial infections of the bowel and perhaps even of ulcerative colitis; sulfathalidine may be better for this purpose because of its slightly lower toxicity.

In surgical patients sulfathalidine is given in doses of 1.5 Gm. every four hours for approximately seven days. Others have commented that a dose half this large is sufficiently effec-

tive and less likely to induce toxic reactions<sup>20</sup> in the rare occasional sensitized patient.

Constipation developing during sulfathalidine therapy is managed by administration of a mild laxative; diarrhea is managed by increasing the dose of sulfathalidine.

Toxic reactions to sulfathalidine are uncommon and are consistently mild; the drug is absorbed in such small quantities that reactions occur only in sensitized patients.

*Streptomycin* (p. 306) is fully as effective an intestinal antiseptic agent as the appropriate sulfonamide drugs. When used for this purpose, it must be given orally, since it is not excreted into the bowel when given parenterally. It is not absorbed from the bowel when administered by mouth. An oral dose of 0.5 Gm. of streptomycin every six hours will reduce the bacterial content of the colon almost to zero within forty-eight hours.

#### URINARY ANTISEPSIS

**Sulfacetimide** (Para aminobenzenesulfonylacetyl-imide).—Because toxic reactions to sulfonamides so often are due to the formation of the therapeutically inactive and highly insoluble acetyl compound which precipitates into the urine, sulfacetimide, which is a sulfonamide already acetylated but therapeutically effective and highly soluble, has been investigated clinically<sup>21</sup> and experimentally. This drug is used chiefly for the treatment of bacillary infections of the urinary tract, in which it is of much value. Since alkalinity favors bacterial growth, the usefulness of other sulfonamides in urinary tract infections is impaired by the necessity of maintaining an alkaline reaction in the urine to prevent precipitation of crystals. Sulfacetimide has the advantage of equal effectiveness and complete solubility in therapeutic amounts in either acid or alkaline urine.

Sulfacetimide is absorbed rapidly after oral administration and is eliminated rapidly into the urine, in which a high concentration of the drug can be maintained. There is little danger of precipitation of crystals in the urinary tract even if the urine is acid in reaction. Toxicity of the drug is very low even during prolonged administration. In spite of its low toxicity, it may be advisable, as Alyea and Parrish<sup>22</sup> have suggested, to ask the patient about previous sulfonamide therapy, especially with

respect to toxic manifestations, to force fluids and administer sodium bicarbonate in conjunction with sulfacetimide, and to observe the renal output and the concentration of the drug in the blood.

For urinary tract infections,<sup>23</sup> sulfathiazole is probably most effective against staphylococci, sulfadiazine against mixed infections, particularly staphylococcic and streptococcic, and sulfacetimide against bacilli. Ordinarily, administration of sulfadiazine for one week will clear the urine of all organisms except bacilli, which then will usually respond to a course of sulfacetimide. If the latter drug proves ineffective, other therapy may be necessary (p. 338).

Sulfacetimide is given in doses of 1.0 Gm. three times a day following meals for three days and then 0.5 Gm. twice daily for seven days. For more chronic or resistant infections, a dose of 1.0 to 1.5 Gm. four times daily may be given for seven days. Sodium bicarbonate is given in the usual alkalinizing dosage, if desired.

### Penicillin

Penicillin, produced by the mold *Penicillium notatum*, is the most effective and least toxic agent available for the treatment of local or general infections due to the staphylococcus, hemolytic streptococcus, or pneumococcus. In other infections, such as those due to the meningococcus or the gonococcus, certain clostridia, *Treponema pallidum* (early stages), and even *Actinomyces bovis*, penicillin is at least as effective as any other agent now in use. The therapeutic effect of penicillin upon disease due to susceptible organisms is astonishingly prompt and the patient's illness sometimes may be over before it is well begun.

Penicillin is produced in several forms, depending upon the method by which the mold is cultivated. Penicillin G is formed chiefly in deep vat culture, while mixtures of penicillin G and X are produced by shallow flask growth. Other forms, present in varying amounts, are penicillin F and K. There is little constant difference in therapeutic effectiveness of the various fractions, except for penicillin K, which is rapidly eliminated from the body and hence is of little use. Penicillin G is the most generally effective fraction and most commercial penicillin now is supplied

in this form. Unless a pure crystalline form of penicillin G is used, the National Research Council<sup>24</sup> recommends increased dosage particularly in treatment of chronic infections such as syphilis.

Penicillin is an organic acid; although it has been synthesized in minute quantities, proof of its chemical structure is not yet conclusive. It is available for clinical use in crystalline form as the sodium, calcium, and potassium salt. The crystalline salts are the least toxic preparations and are now in general use. The chief disadvantages of the sodium salts are that it is hygroscopic and must be supplied in ampules and that it is somewhat less stable than other penicillin salts. Solutions of sodium penicillin for parenteral use can be kept in the refrigerator (below 10° C.) for a week; solutions for local application can be kept without too much deterioration either at room temperature for a week or in the refrigerator for two weeks. Crystalline penicillin is much more stable than the earlier powdered mixed forms supplied for parenteral use. The calcium salt is the most stable and is best adapted to oral administration.

Following parenteral administration, penicillin is absorbed promptly into the blood stream. It is carried rapidly throughout the body and diffuses in satisfactory therapeutic concentrations into all the tissues except those of the central nervous system. The drug enters the infected peritoneal cavity in useful amounts when administered parenterally in large doses, but infections of other body cavities (pleural cavity, cranial cavity, spinal canal, joint cavities) require supplementary local injections of penicillin. Penicillin is excreted unchanged in the urine at a rapid rate.

With respect to pharmacologic effects, penicillin is almost entirely inert; it has little action upon the tissues and organs of the body and its toxicity is very low. Except for an occasional case of sensitivity developing following its use, penicillin is a close approximation to the ideal therapeutic agent, having an extremely high antibacterial effect on susceptible organisms and a very low degree of toxicity.

Penicillin is more rapidly effective than sulfonamides. It probably exerts its effect upon susceptible organisms by preventing their multiplication rather than by interfering with

their growth; eradication of the infection then is completed by the natural defense processes<sup>23</sup> of the body. Inadequate dosage of penicillin may result in development of penicillin-fastness or resistance by the infecting organisms. Since penicillin is ordinarily used systemically only in severe infections, full doses are advisable from the beginning of treatment. In other cases, naturally resistant strains may occur even among susceptible organisms. Penicillin-fastness and sulfonamide-fastness are not related, so that a susceptible organism unaffected by one drug usually can be controlled by adequate doses of the other. In especially severe infections it is sometimes advisable to use penicillin and a sulfonamide together. Lack of response to such therapy may indicate the presence of a focus requiring surgical drainage.

Certain bacteria, particularly the gram-negative intestinal bacteria, produce an enzyme called *penicillinase*, which inactivates penicillin. Penicillinase is produced also by some strains of *Pseudomonas aeruginosa* (*Bacillus pyocyaneus*) and by *Aerobacter aerogenes*. None of these organisms is susceptible to penicillin and the presence of any of them as a contaminant in mixed infections will decrease the effect of penicillin upon the susceptible organisms present, whether the drug is administered parenterally or locally. Penicillin, unlike the sulfonamides, is not greatly inhibited in its effect by the presence of blood, serum, pus, or necrotic tissue.

**Administration.** — Penicillin is ordinarily measured in units rather than in milligrams for dosage purposes. The original Oxford (or Florey) unit was described as the minimal amount of penicillin necessary to inhibit completely growth of a standard strain of *Staphylococcus aureus* in 50 c.c. of beef broth. More recently an international unit<sup>24</sup> was established, approximately equal to the Oxford unit, but described as the penicillin activity present in 0.6 mg. of the international master standard of pure crystalline sodium penicillin G. This standard crystalline penicillin has been shown by repeated assay to have a potency of 1,650 units per milligram. Each of the various commercial penicillin products is labelled with the penicillin content in units. The purity of any commercial sodium penicillin G may be ascertained by comparison of its potency with that of the international standard.



Penicillin is usually given dissolved in sterile normal salt solution, 5 per cent dextrose solution, or distilled water. The drug is eliminated rapidly by the kidneys, about 60 per cent being excreted during the first half hour following absorption into the blood. Intravenous injection results in a rapid rise in the concentration of penicillin in the blood, followed by a prompt and equally rapid fall, as the drug is lost in the urine. For this reason, penicillin is not ordinarily given intravenously. If intravenous injection is considered advisable, however, as in a profoundly ill patient, solutions of penicillin may be injected in frequently repeated doses by means of a syringe (10,000 to 50,000 units per cubic centimeter) or by continuous infusion (25 to 50 units per cubic centimeter). Absorption into the blood stream is slower and the therapeutic level of the drug in the blood is maintained for a longer time if repeated doses are given intramuscularly (10,000 to 50,000 units per cubic centimeter). Fleming and co-workers<sup>27</sup> have recommended administration of small doses (15,000 units) intramuscularly every two or three hours rather than larger doses at longer intervals, since a full therapeutic level can be maintained more steadily as well as more economically by small frequent doses. For treatment of acute infections, the drug therefore is best given intramuscularly in doses of 15,000 to 30,000 units every three hours. Further increase in dosage and prolongation of interval tends to waste the drug without increasing the therapeutic effect. These doses, however, are fully effective only in acute infections due to organisms specifically susceptible to penicillin. Mixed infections such as peritonitis or chronic infections such as empyema may require massive doses of penicillin (p. 448), up to 100,000 units every two hours. Regulation of dosage must be done in accordance with clinical response, since methods for obtaining determinations of the penicillin level in the blood are unsatisfactory.

*Toxic reactions* to penicillin administered orally or intramuscularly are mild and are generally nonspecific, although typical sensitization reactions do occur. The reactions most commonly seen include chills, pain at the site of injection, headache, flushing, an unpleasant taste during the absorption of the drug, slight fever of short duration, urticaria, dermatitis, and phlebitis following intravenous administration. Skin reactions of all types, from erythema and urticaria to exfoliative dermatitis,

have been observed. Except for the occasional sensitization reactions, these mild toxic effects have become uncommon as the use of pure crystalline penicillin has become universal. Toxic sensitization reactions to penicillin respond well to the anti-histamine drugs (Pyribenzamine, Benadryl) in the usual dosage of 50 to 100 mg., repeated as necessary.

**Dosage and Indications.**—For treatment of unusually severe infections, it is advisable to produce a therapeutic concentration of penicillin in the blood stream as quickly as possible. A dose of 25,000 units of the drug may be given intravenously, with the simultaneous administration of 50,000 units of penicillin intramuscularly. Proper blood levels of the drug are then maintained by intramuscular administration of at least 25,000 units every two hours or 50,000 units every three hours. Less severe infections are treated in the same way, a smaller dosage being satisfactory. Absorption of penicillin from the area into which it has been injected may be delayed somewhat by local application of an ice bag or hastened by application of heat. Continuous intramuscular injection of penicillin has been advocated for treatment of severe infections, but results obtained by doses given every two or three hours apparently are just as satisfactory.

Infections of the body cavities can be treated by the use of penicillin locally as well as systemically. Solutions of penicillin containing from 10,000 to 25,000 units of the drug per cubic centimeter may be injected into the thoracic cavity in treatment of empyema or following operation, into the peritoneal cavity following operation, into the spinal canal or cranial cavity, or into joint cavities for the treatment of suppurative arthritis. Other uses for penicillin in surgery include its use in the preoperative and postoperative care of patients undergoing thoracic or plastic surgery, its topical application in solution (1,000 units per cubic centimeter) to open wounds or granulating surfaces (p. 481), and its direct injection into and around infected areas, such as furuncles or carbuncles (p. 305).

Penicillin has been combined with various vehicles to delay absorption and make possible a sustained therapeutic level in the blood by doses administered at long intervals. The preparation of this type most widely used at present consists of calcium

penicillin suspended in a mixture of refined peanut oil and white wax<sup>21,22</sup> (from 3.0 to 4.9 per cent wax). The suspension is obtainable in a concentration of 300,000 units per cubic centimeter and is given intramuscularly in minimum dosage of 300,000 units every twenty-four hours. Since absorption is slow, successive injections are given in different areas, using the deltoid insertion, the triceps, and the upper outer quadrant of each buttock. Crystalline procaine-penicillin in oil is a recent modification. Obviously, penicillin in oil and wax is not safe for intravenous use.

Penicillin is inactivated by hydrochloric acid in the stomach and by penicillinase in the intestine. For this reason, oral administration of the drug is not as satisfactory as parenteral injection. In less severe infections, however, enough penicillin is absorbed following the administration of large doses by mouth to produce effective levels in the blood stream. Special preparations for oral use are available, buffered against the hydrochloric acid of the gastric juice by addition of sodium citrate or citric acid or of an aluminum hydroxide compound. The tablets contain 50,000 units each and are given to supply doses of from 50,000 to 100,000 units of penicillin every two to three hours. They are most effective if given when the stomach is empty, or at least a half hour before meals and not sooner than an hour and a half after meals.

For topical use, a finely powdered calcium penicillin is available in individual packages containing 10,000 to 50,000 units of the drug. Solutions of topical penicillin are applied locally in dilutions usually of 1,000 units per cubic centimeter. It is often advisable to accompany topical application of penicillin with systemic administration of the drug. Since penicillin is a bacteriostatic agent rather than a bactericide, irrigations are not entirely effective. The solution must remain in contact with the infected surface for from six to twelve hours to exert a therapeutic effect.

Indications for use of penicillin according to the best information available at present are listed as follows in a special article<sup>23</sup> by the Committee on Chemotherapeutics and Other Agents of the National Research Council:

## GROUP I INDICATIONS

1. All staphylococcic infections with and without bacteremia:
  - Acute and chronic osteomyelitis.
  - Carbuncles—soft tissue abscesses.
  - Meningitis.
  - Cavernous or lateral sinus thrombosis
  - Pneumonia—empyema.
  - Carbuncle of kidney.
  - Wound infections—burns.
  - Endocarditis.
2. All cases of clostridia infections:
  - Gas gangrene.
  - Malignant edema.
3. All hemolytic streptococcic infections with bacteremia and all serious local infections:
  - Cellulitis.
  - Mastoiditis with intracranial complications, i.e. meningitis, sinus thrombosis and so on.
  - Pneumonia and empyema.
  - Puerperal sepsis.
  - Peritonitis.
  - Endocarditis.
4. All anaerobic streptococcic infections:
  - Puerperal sepsis.
  - Localized infections elsewhere
5. All pneumococcic infections of:
  - Meninges.
  - Pleura.
  - Endocardium.
  - All cases of sulfonamide-resistant pneumococcic pneumonia.
6. All gonococcic infections.
7. All cases of anthrax.
8. All cases of chronic pulmonary suppuration in which surgical treatment is contemplated.
9. All meningococcic infections failing to respond to sulfonamides.
10. All cases of bacterial endocarditis due to susceptible organisms.
11. Erysipeloid (swine erysipelas).
12. Vincent's infection.
13. Prophylactic use in prevention of possible secondary infection following tonsillectomy and tooth extraction in cases with a history of rheumatic fever or in rheumatic heart disease, in congenital heart disease and in other conditions in which secondary infection may occur (infected teeth; tonsils).

## GROUP II INDICATIONS

Penicillin has also been found to be an effective agent in the following diseases, but its position has not been definitely defined and will require additional experimental work

1. Syphilis
2. Actinomycosis.
3. Diphtheria, in conjunction with antitoxin.

## GROUP III CONDITIONS OF QUESTIONABLE VALUE

Penicillin is of questionable value in mixed infections in which the predominating organism is of the gram negative flora—i.e.:

1. Ruptured appendix with peritonitis.
2. Liver abscesses.
3. Urinary tract infections due to *Escherichia coli*
4. It is also of questionable value in rat bite fever due to *Streptobacillus moniliformis*.

## GROUP IV CONDITIONS IN WHICH PENICILLIN IS INEFFECTIVE

1. All gram negative bacillary infections:
  - Typhoid—paratyphoid.
  - Dysentery.
  - Escherichia coli*.
  - Hemophilus influenzae*.
  - Bacillus proteus*.
  - Bacillus pyocyaneus*.
  - Brucella melitensis* (undulant fever).
  - Pasteurella tularensis* (tularemia)
  - Friedländer's bacillus.
2. Tuberculosis.
3. Toxoplasmosis.
4. Histoplasmosis.
5. Acute rheumatic fever.
6. Lupus erythematosus diffuse.
7. Infectious mononucleosis
8. Pemphigus
9. Hodgkin's disease.
10. Acute and chronic leukemia.
11. Ulcerative colitis.
12. Coccidioidomycosis.
13. Malaria.
14. Poliomyelitis.
15. Blastomycosis.
16. Nonspecific iritis and uveitis
17. Moniliasis.
18. Virus infections.
19. Cancer.

To the above list of indications may be added the use of penicillin in treatment of malignant neutropenia (agranulocytosis) to prevent the development of secondary infections (p. 280).

The injection of penicillin directly into and around an infected region, such as a carbuncle or an area of acute cellulitis, has been advocated. Although injection of fluid into an infected area apparently is in contradiction to fundamental surgical principles, introduction of penicillin in this way may produce rapid relief of pain and prompt subsidence of inflammation, often without need for surgical drainage. The method of treatment, however, has not come into general use.

For *local injection* into a regional tissue infection caused by a susceptible microorganism, penicillin in sterile normal salt solution in concentrations of 10,000 to 50,000 units per cubic centimeter is used. The method of injection depends on the type, location, and extent of infection. A syringe is used, with a needle of appropriate size, and injection is begun in normal tissue about 1 cm. beyond any evident redness or tenderness. After a small amount of penicillin solution is deposited around the area of the puncture, the needle is inclined toward the infected region and introduced into this area. Injection is continued slowly as the needle progresses toward the center of the lesion. From one to four punctures are necessary, according to the size of the area involved. For small infections requiring a single injection, 1 c.c. containing 50,000 units of penicillin is sufficient; for larger areas such as a carbuncle, two to four punctures are required, with introduction of 1 to 2 c.c. of solution (15,000 to 25,000 units per cubic centimeter) through each puncture. One injection a day is usually sufficient, and treatment is rarely necessary for more than three days. Simultaneous systemic administration of penicillin is necessary only when there is evidence of regional or generalized infection with spread to the regional lymphatics or to the blood stream.

Injection of penicillin into the already tense infected tissues is severely painful, especially in finger infections, and usually requires general anesthesia for a few moments. Local nerve block is quite unsatisfactory. From the standpoint of the surgeon, intravenous sodium pentothal is the best anesthetic, with nitrous oxide and oxygen the second choice. For a few minutes following injection of penicillin solution, the infected area is

more painful than before because of the temporarily increased tissue tension. Within a surprisingly short time, the pain subsides and the patient becomes comfortable. Evidences of acute inflammation rapidly fade away, and regression and healing follow promptly. It is sometimes necessary to make a small incision over a fluctuant area to evacuate pus, but in many cases the pus may be either aspirated with a large needle or simply allowed to disappear spontaneously by absorption. Various reports have appeared, such as that of Rose and Hurwitz,<sup>30</sup> expressing complete satisfaction with this mode of treatment. Although introduction of penicillin directly into the infected area is advocated generally, the injection of the solution into the uninfected tissues immediately around the lesion causes less pain, produces equally good results, and appears to be more consistent with basic surgical principles.

### Streptomycin

Like penicillin, streptomycin is an antibiotic substance produced by a living organism. Similarly, too, it combines low toxicity with high therapeutic effect in infections due to certain susceptible microorganisms. The drug was studied and first isolated in 1944 by Waksman and his group, who extracted it from cultures of certain strains of an actinomyces (*Streptomyces griseus*) found normally in soil. Large-scale production is at present accomplished by growing the organism in sterilized soil and inoculating the resultant colony into large fermentation tanks filled with a special culture medium.

While penicillin is most active against gram-positive organisms, particularly staphylococci, streptomycin is most effective against gram-negative bacilli. Dramatic therapeutic results have been obtained by use of streptomycin in severe infections due to organisms of this group.

Because of the scarcity of streptomycin during the months immediately following its isolation, the distribution of the drug was controlled closely by the National Research Council<sup>31</sup> for two years, until reports of its use in a thousand cases of susceptible and possibly susceptible infections were studied as a whole.

The chemical structure of streptomycin is well known and crystalline salts have been prepared. The drug is currently

supplied as the sulfate, the hydrochloride, or the calcium-chloride complex, all of which are freely soluble in water and are relatively stable. Commercial preparations other than the pure crystalline streptomycin base are labelled to indicate the comparative potency with respect to the pure base. Earlier reports used the "S unit" as a measure of streptomycin activity, but this unit has been discarded in favor of a standard of activity established on the weight of pure streptomycin base. According to the present standard, 1.0 mg. of pure crystalline streptomycin is equivalent in activity to 1,000 "S units."

**Administration.**—Following oral administration, streptomycin is neither inactivated in the gastrointestinal tract nor readily absorbed from it. Oral administration of the drug therefore is unsatisfactory for treatment of systemic infections, although it will result in bacteriostasis and reduction of susceptible gram-negative organisms in the bowel. Following parenteral injection, streptomycin is quickly absorbed into the blood stream and carried throughout the body. Diffusion into all the tissues is rapid, although the drug does not pass in satisfactory amounts into the cerebrospinal fluid or pleural cavity, nor does it pass into the bowel lumen. It does, however, diffuse into the peritoneal cavity in therapeutic concentrations even in the presence of peritonitis. Streptomycin is excreted more slowly than penicillin, and constant therapeutic levels of the drug in the blood stream can be maintained without difficulty. It is excreted unchanged into the urine, in which it may reach a high concentration, and it is also excreted to some extent into the bile.

Streptomycin is best given by intermittent intramuscular injection. This mode of administration is the most convenient, the least painful, and the most effective. Absorption of the drug is fairly rapid, therapeutic levels of streptomycin appearing in the blood within one to three hours after injection of the first dose. Excretion of the drug is relatively slow, so that intramuscular injection of a standard dose every three or four hours will not only maintain a steady and satisfactory therapeutic level, but will produce a slight continuous rise in concentration of streptomycin in the blood up to a maximum level for the dosage employed. Doses of 0.1 to 0.2 Gm. of streptomycin given



intramuscularly every three hours will maintain an average concentration in the blood of from 2 to 6 micrograms per cubic centimeter. Blood levels of streptomycin following standard doses vary widely among different patients, and susceptibility of various organisms and even of various strains of an organism varies within wide limits. Determination of the proper dosage level of streptomycin therefore bears a closer relation to the tolerance of the particular infecting microorganisms than to the establishment of an arbitrary concentration of the drug in the blood.

Penicillin and streptomycin are compatible in solution and can be given simultaneously from the same syringe, when combined therapy is indicated. Such a solution should be made fresh daily.

The usual sites for intramuscular injection (deltoid, anterolateral thigh, upper outer quadrant of the buttock) are employed and successive doses are rotated among different regions to prevent prolonged discomfort. Solutions of streptomycin are somewhat irritating and may be productive of pain on parenteral administration. Injection is therefore made slowly. A concentration of 200 mg. of streptomycin base per cubic centimeter of normal salt solution is usually employed, although solutions for intrathecal injection should contain only 10 to 20 mg. per cubic centimeter. Pain following injection of streptomycin can be minimized by addition of a local anesthetic to the solution; for example, enough procaine to make 0.20 per cent (1.0 c.c. of 1 per cent procaine to each 4.0 c.c. of streptomycin solution).

Intravenous administration of streptomycin offers no advantage and may be followed by a prompt toxic reaction. Subcutaneous injection is somewhat more painful than intramuscular injection but may be employed. Oral administration is quite unsatisfactory for treatment of systemic infections and is used only occasionally in therapy of certain gastrointestinal infections or for reduction of intestinal flora prior to surgical operations on the bowel. Streptomycin can be given effectively by aerosol or nebulizer inhalation combined with systemic therapy for treatment of bronchial or pulmonary infections due to susceptible organisms.

**Indications.**—Although it is possible that high concentrations of streptomycin may exert some bactericidal effect, the

action of the drug on susceptible organisms is almost entirely bacteriostatic, and final eradication of the infection is accomplished by the natural defenses of the body.

TABLE IV. STREPTOMYCIN IN THE TREATMENT OF INFECTIONS  
SUMMARY OF RESULTS IN 1,000 CASES

(From Keefer and others: J. A. M. A. 132: 4, 1946.)

	NUMBER OF PATIENTS	RESULTS			
		RECOV- ERED	IM- PROVED	NO EFFECT	OED
Urinary tract infections	409	171	145	84	9
H. influenzae meningitis	100	66	14	3	17
Bacteremia	91	49	12	4	26
Tularemia	67	63		3	1
Pulmonary infections	44	15	14	7	8
Brucellosis	45	..	30	15	
Typhoid	51	..	51		
Salmonella	26	10	2	6	8
Peritonitis	53	36	3	2	12
Meningitis due to gram- negative organisms other than H. influenzae	14	5	5	..	4
Shigella dysenteries	2	2			
Miscellaneous infections	98	36	29	30	3
Totals	1,000	453	305	154	88

Streptomycin can neither be substituted for penicillin nor used interchangeably with it. Although streptomycin may produce slight clinical improvement in some infections which also respond to penicillin therapy, the drugs are not equally effective against any specific organism, and the more effective drug is to be preferred. According to current information, streptomycin is highly effective in the treatment of bacteremia, urinary tract infection, or meningitis caused by gram-negative bacilli and in supplementary treatment of peritonitis and of empyema due to organisms of these types. It is also of great value in the treatment of tularemia and of pulmonary infections due to *Hemophilus influenzae* or to Friedländer's bacillus.

TABLE V. RANGE IN SENSITIVITY OF GRAM-POSITIVE AND GRAM-NEGATIVE BACTERIA AND ACTINOMYCETES TO THE BACTERIOSTATIC ACTION OF STREPTOMYCIN\*

(From Keefer and others: J. A. M. A. 132: 70, 1946.)

	MICROGRAMS PER CUBIC CENTIMETER	
Gram-negative organisms		
<i>Aerobacter aerogenes</i>	0.5	64.0
<i>Bacillus anthracis</i>	0.375	
<i>Brucella abortus</i>	0.5	3.75
<i>Brucella melitensis</i>	0.5	
<i>Brucella suis</i>	0.5	
<i>Eberthella typhi</i>	1.0	37.5
<i>Erysipelothrix rhusiopathiae</i>	2.5	
<i>Escherichia coli</i>	0.3	3.75†
<i>Escherichia communior</i>	1.0	4.0
<i>Hemophilus influenzae</i>	1.56	5.0
<i>Hemophilus pertussis</i>	1.25	3.0
<i>Klebsiella ozogenes</i>	0.375	1.5
<i>Klebsiella pneumoniae</i>	0.625	256
<i>Malleomyces mallei</i>	10.0	>10.0
<i>Neisseria gonorrhoeae</i>	5.0	
<i>Neisseria intracellulæris</i>	5.0	
<i>Pasteurella leptiseptica</i>	0.5	2.5
<i>Pasteurella pestis</i>	0.75	1.5
<i>Pasteurella tularensis</i>	0.15	0.3
<i>Proteus vulgaris</i>	0.4	3.2
<i>Pseudomonas aeruginosa</i> †	2.5	25.0
<i>Salmonella aertrycke</i>	4.0	10.0
<i>Salmonella enteritidis</i>	0.5	
<i>Salmonella schottmüllerii</i>	2.0	
<i>Salmonella suispestifer</i>	60.0	
<i>Shigella paradyserteriae</i>	0.25	3.75
<i>Vibrio comma</i>	6.0	37.5
Gram-positive organisms		
<i>Actinomyces bovis</i>	3.75	
<i>Clostridium butyricum</i>	8.34	
<i>Clostridium septicum</i>	>105	
<i>Clostridium sordelli</i>	>105	
<i>Clostridium tetani</i>	>104	
<i>Clostridium welchii</i>	>104	
<i>Corynebacterium diphtheriae</i>	0.375	3.75
<i>Diplococcus pneumoniae</i>	8.0	
<i>M. tuberculosis, var. hominis</i>	0.15	

TABLE V. RANGE IN SENSITIVITY OF GRAM-POSITIVE AND GRAM-NEGATIVE BACTERIA AND ACTINOMYCETES TO THE BACTERIOSTATIC ACTION OF STREPTOMYCIN\*—CONT'D

	MICROGRAMS PER CUBIC CENTIMETER	
<i>Staphylococcus aureus</i> ‡	0.5	>16 0
<i>Streptococcus fecalis</i>	50 0	
<i>Strept. hemolyticus</i>	2.0	>16 0
<i>Strept. lactis</i>	4 0	
<i>Strept. salivarius</i>	5 0	25 0
<i>Strept. viridans</i>	>16	120

\*Micrograms of streptomycin per cubic centimeter of suitable medium required to inhibit growth.

‡Some colon bacilli have been reported to require 300 to 50,000 micrograms per cubic centimeter to inhibit growth.

†Of a group of *Ps. aeruginosa* and *Ps. fluorescens* (by Hirschfeld) some required over 256 micrograms per cubic centimeter to inhibit growth.

§Some staphylococci have been reported (by Hirschfeld) to require over 256 micrograms per cubic centimeter to inhibit growth.

The effect of streptomycin in vitro upon the common pathogenic microorganisms is given in detail<sup>11</sup> in Table IV and the effect in vivo upon various clinical infections due to gram-negative organisms in Table V. In general, organisms inhibited in vitro by low concentrations of streptomycin are also susceptible to the drug in vivo, while organisms requiring high concentrations of the drug to inhibit growth in culture are also resistant to the drug clinically. The effect of streptomycin upon susceptible organisms in vitro is not observed to a proportionate degree in the treatment of clinical infections for several reasons. First, the resistance of susceptible organisms to streptomycin is increased from four to eight times by the presence of blood or serum. Enough streptomycin must be administered therefore to maintain a concentration of the drug in the blood up to eight times that required for inhibition of growth of the organism in vitro. Second, different strains of a susceptible organism may vary widely in resistance to streptomycin. The range in sensitivity given in Table V indicates the wide limits in response to the drug that may occur. If possible, the organism

responsible for the clinical infection should be tested in culture with respect to its individual sensitivity to streptomycin before treatment is begun and the therapeutic dosage plan regulated accordingly. Third, susceptible organisms may develop "fastness" or resistance to streptomycin rapidly if insufficient doses of the drug are used. Full therapeutic dosage must be used from the outset of treatment in order to destroy all the infecting organisms as quickly as possible. Bacteria remaining after the first one to three days of streptomycin treatment may develop so much tolerance to the drug that even huge doses subsequently will fail to eradicate the infection. Fourth, insufficient doses of streptomycin at the beginning of treatment actually may increase the severity of the infection, particularly if naturally resistant strains are present. Finally, as the bacteria susceptible to streptomycin are destroyed, organisms of other types may multiply rapidly and invade the diseased tissues, causing further damage.

For these reasons, certain precautions should be taken, if at all possible, before beginning treatment with streptomycin. The infecting organism should be identified in culture, with simultaneous tests made to determine roughly its degree of sensitivity to streptomycin. Doses of streptomycin should be used that will afford a constant streptomycin level in the blood at least four to eight times that required to inhibit growth of the organism in culture. The maximum useful<sup>22</sup> dosage of the current preparations of streptomycin that can be tolerated without production of toxic symptoms averages 3.0 Gm. a day (0.5 Gm. intramuscularly every four hours or 0.375 Gm. every three hours). On this dosage plan, levels of 16 micrograms or more of streptomycin per cubic centimeter of blood can be maintained. The average dosage of streptomycin commonly used varies from 1.0 to 3.0 Gm. a day (0.167 to 0.50 Gm. intramuscularly every four hours or 0.125 to 0.375 Gm. every three hours) for from five to fourteen days. In all cases, full therapeutic dosage is instituted with the first dose in an effort to destroy all the infecting bacteria within the first day or two of treatment, although administration of the drug is continued for several days after disappearance of all signs of infection.

*Urinary tract infections* due to *Escherichia coli*, *Aerobacter aerogenes*, or *Proteus vulgaris* are particularly susceptible to streptomycin; infections due to *Pseudomonas aeruginosa* are somewhat less responsive<sup>33</sup> to the drug. Doses of 1.0 to 2.0 Gm. a day (0.17 to 0.33 Gm. intramuscularly every four hours) for four to five days usually are sufficient; smaller doses may permit rapid development of tolerance to the drug, after which even very large doses are likely to prove ineffective. The presence of urinary stones, foreign bodies, tumors, or obstructions in the urinary tract may so interfere with the effect of streptomycin as to render it useless. It is advisable to make sure that free unobstructed drainage of the urinary tract exists before administration of the drug is begun. Mixed infections of the urinary tract respond less well than infections due to a single organism.

*Bacteremia* due to gram-negative bacilli responds well to streptomycin, doses of 2.0 to 3.0 Gm. each day (0.250 to 0.375 Gm. intramuscularly every three hours) for twelve days usually being sufficient. As in any extremely severe illness, however, not all patients with bacteremia will respond to streptomycin treatment. The presence of profound toxicity or of debilitating chronic disease will sometimes prevent a favorable response to the drug, even though the organism is of a susceptible type. When the primary lesion from which the microorganism enters the blood stream is in the urinary tract, an especially satisfactory response can be expected. In such a case, streptomycin will not only control the bacteremia, but may eradicate the local infection as well.

Streptomycin is apparently of considerable value in treatment of *infectious peritonitis*, especially the type secondary to perforative appendicitis. In treatment of bacterial peritonitis, streptomycin is given in doses of 3.0 Gm. daily (0.375 Gm. intramuscularly every three hours) together with other drugs as indicated. Penicillin, used simultaneously, should be given in massive doses (p. 448) because of its partial inactivation by penicillinase (secreted by contaminating intestinal bacteria). Streptomycin is particularly useful in spreading peritonitis when the response to penicillin and sulfadiazine is unsatisfactory.

Certain diseases primarily of medical interest also respond well to treatment with streptomycin, with striking reduction in morbidity and mortality. *Tularemia* responds promptly and

completely to streptomycin, which is by far the most effective agent available for treatment of this disease in any of its forms. *Meningitis* due to *Hemophilus influenzae* can be cured in many instances by intrathecal administration of streptomycin, and *acute pneumonitis* due to gram-negative organisms (*Hemophilus influenzae* or Friedländer's bacillus) responds well to streptomycin, although the patient's recovery is less likely if this infection has become chronic.

**Toxic Effects.**—Intramuscular administration of streptomycin may produce an aching pain at the site of injection, usually of short duration but sometimes lasting from one dose to the next. This untoward effect can be minimized by use of a local anesthetic drug together with the streptomycin solution. With newer pure preparations, this effect is much less evident.

Headache, flushing of the face, transient fall in blood pressure, nausea, and even vomiting has occurred following administration of streptomycin intravenously or in large doses intramuscularly. These histaminelike effects of the drug are due to impurities, and while severe reactions occurred with the use of the earlier preparations, they are no longer common.

Other more serious toxic reactions are rare. Streptomycin exhibits a neurotoxic<sup>11,44</sup> effect on the auditory nerve in some patients, tinnitus or vertigo appearing either early or late in the course of treatment. Although these symptoms are transitory and disappear after several days or weeks, the possibility of permanent damage to the eighth nerve has not yet been ruled out. Appearance of tinnitus, vertigo, or slight deafness during the course of streptomycin therapy therefore requires immediate discontinuance of the drug unless the infecting organism is known to be susceptible and the infection is seriously threatening the patient's life. True sensitization to streptomycin has been reported, with appearance of a skin rash, fever, and eosinophilia within a week after institution of therapy. Toxic manifestations of this type also require immediate withdrawal of the drug. Desensitization may be tried, if further dosage is advisable.

### References

1. Fleming, A.: On Specific Antibacterial Properties of Penicillin and Potassium Tellurite; Incorporating Method of Demonstrating Some Bacterial Antagonisms, *J. Path. & Bact.* 35: 831, 1932.

2. Woods, D. D.: Relationship of P-Aminobenzoic Acid to Mechanism of Action of Sulphanilamide, *Brit. J. Exper. Path.* 21: 74, 1940.
3. Kohn, H. I.: Antagonists (Excluding P-Aminobenzoic Acid), Dynamists and Synergists of Sulfonamides, *Ann. New York Acad. Sc.* 44: 503, 1943.
4. Henry, R. J.: The Mode of Action of Sulfonamides, *Bact. Rev.* 7: 175, 1943.
5. Bratton, A. C., and Marshall, E. K., Jr.: New Coupling Component for Sulfanilamide Determination, *J. Biol. Chem.* 128: 537, 1939.
6. LaRosa, W. V.: Use of Test Paper for Rapid Estimation of Sulfonamides in Blood and Other Body Fluids, *J. Lab. & Clin. Med.* 30: 531, 1945.
7. Rohr, J. H., and Christopher, F.: Administration of Alkalis in Sulfadiazine Therapy, *Surg., Gynec. & Obst.* 78: 515, 1944.
8. Abeshouse, B. S.: Renal Decapsulation; Review of Literature and Report of 10 Cases, *J. Urol.* 53: 27, 1945.
9. Lyons, Champ: Chemotherapy in the Management of Wounds, *J. A. M. A.* 133: 215, 1947.
10. Circular Letter Orders 160, United States War Department, Washington, D. C., Government Printing Office, June 1, 1945, par. 5.
11. Meloney, F. L., and Whipple, A. O.: Statistical Analysis of Study of Prevention of Infection in Soft Part Wounds, Compound Fractures, and Burns With Special Reference to Sulfonamides, *Surg., Gynec. & Obst.* 80: 263, 1945.
12. Mueller, R. S.: Local Use of Sulfanilamide in Treatment of Acute Appendicitis; Review of 1,481 Cases, *Ann. Surg.* 122: 625, 1945.
13. Shaffer, B., Lentz, J. W., and McGuire, J. A.: Sulfathiazole Eruptions; Sensitivity Induced by Local Therapy and Elicited by Oral Medication; Report of 4 Cases With Some Allergic Studies, *J. A. M. A.* 123: 17, 1943.
14. Lehr, D.: Prevention of Renal Complications by Therapeutic Employment of Sulfonamide Mixtures; Sulfathiazole-Sulfadiazine Combination, *J. Urol.* 55: 548, 1946.
15. Flippin, H. R., and Reinhold, J. G.: An Evaluation of Sulfonamide Crystalluria, *Ann. Int. Med.* 25: 433, 1946.
16. Poth, E. J., and Knotts, F. L.: Clinical Use of Succinylsulfathiazole, *Arch. Surg.* 44: 208, 1942.
17. Poth, E. J.: Succinylsulfathiazole and Phthalylsulfathiazole in Surgery of Colon, *Surgery* 17: 773, 1945.
18. Dixon, C. F., and Benson, R. E.: Closure of Colonic Stoma; Improved Results With Combined Succinylsulfathiazole and Sulfathiazole Therapy, *Ann. Surg.* 120: 562, 1944.
19. Poth, E. J., and Ross, C. A.: Clinical Use of Phthalylsulfathiazole, *J. Lab. & Clin. Med.* 29: 785, 1944.
20. Cave, H. W.: Discussion of Streicher, *J. A. M. A.* 129: 1082, 1945.
21. Welebir, F., and Barnes, W.: The Use of Sulfacetimide in Bacillary Infections of the Urinary Tract, *J. A. M. A.* 117: 2132, 1941.
22. Alyea, E. P., and Parrish, A. A.: Sulfacetimide and Sulfadiazine Therapy in Urinary Tract Infections, *South. M. J.* 36: 719, 1943.



23. Lehr, D.: Experimental and Clinical Studies With Sulfacetamide (P-Aminobenzenesulfonylacetylamide). Toxicity and Efficiency in Bacillary Infections of Urinary Tract; Experimental Studies, *J. Urol.* 54: 87, 1945.
24. Report of the Council on Pharmacy and Chemistry: Penicillin Facts and Figures, *J. A. M. A.* 131: 1423, 1946.
25. Hobby, G. L., and Dawson, M. H.: Bacteriostatic Action of Penicillin on Hemolytic Streptococci in Vitro, *Proc. Soc. Exper. Biol. & Med.* 56: 178, 1944.
26. Report: Recommendation of International Conference on Penicillin, *Science* 101: 42, 1945.
27. Fleming, A., Young, M. Y., Suchet, J., and Rowe, A. J. E.: Penicillin Content of Blood Serum After Various Doses of Penicillin by Various Routes, *Lancet* 2: 621, 1944.
28. Keefer, C., Herwick, R. P., Van Winkle, W., and Putman, L. E.: New Dosage Forms of Penicillin. Statement Concerning Certifiable Penicillin Products, Including Recommended Indications, Dosages, and Precautions, *J. A. M. A.* 128: 1161, 1945.
29. Romansky, M. J.: The Current Status of Calcium Penicillin in Beeswax and Peanut Oil, *Am. J. Med.* 1: 395, 1946.
30. Rose, D., and Hurwitz, D.: Regional Injection of Penicillin in Local Infections. Preliminary Report, *New England J. Med.* 234: 291, 1946.
31. Keefer, C. S., and others, Committee on Chemotherapeutics and Other Agents, National Research Council: Streptomycin in the Treatment of Infections, *J. A. M. A.* 132: 4, 70, 1946.
32. Pulaski, E. J., and Sprinz, H.: Streptomycin in Surgical Infections. I. Laboratory Studies, *Ann. Surg.* 125: 194, 1947.
33. Pulaski, E. J., and Amspacher, W. H.: Streptomycin Therapy in Urinary Tract Infections, *Surg., Gynec. & Obst.* 85: 107, 1947.
34. Fowler, E. P., Jr., and Seligman, E.: Otic Complications of Streptomycin Therapy, *J. A. M. A.* 133: 87, 1947.

## CHAPTER 12

### MINOR POSTOPERATIVE COMPLICATIONS

The average patient, if properly prepared before operation and properly managed during the early postoperative period, usually will pass through an uneventful convalescence, marked by no untoward incidents of a serious nature. There are, however, certain disturbances of function that are common following surgical procedures, particularly upon the abdomen, which are not severe enough in their consequences to be considered as complications but are frequent enough and annoying enough to demand prompt attention. Such conditions, if not detected and treated during incipiency, may develop into actual complications of a more serious and dangerous nature. Some functional disturbances of the post-operative period, such as prolonged vomiting, inability to void, and intestinal distention, tend to occur to a somewhat more marked degree in individuals who are emotionally unstable or apprehensive. If the complete confidence of such patients can be gained and their fears dissipated, many of the physiologic upsets of the postoperative period will respond to treatment with surprising ease.

#### Conjunctivitis

Conjunctivitis may occur after operation as a result of irritation by the anesthetic. Frequent irrigations with boric acid solution (4 per cent) and applications of warm boric acid dressings to the eyes will generally relieve the condition. With the steadily improving techniques of anesthetic administration, this minor complication, usually secondary to open drop ether anesthesia, is fast becoming uncommon.

#### Pharyngitis

Pharyngitis as a result of anesthetic irritation develops within one or two days after operation and usually disappears as soon as the patient is able to take sufficient fluids by mouth. A mild infectious pharyngitis or early coryza present and unobserved before operation, however, may be aggravated into an

acute upper respiratory tract inflammation by administration of an inhalation anesthetic, particularly if an airway or an intra-tracheal tube is used. This complication, mild in itself, may be responsible for the development of a spreading bronchitis or pneumonitis and therefore must be treated energetically as soon as it develops.

Inhalations of steam, either pure or medicated, will relieve pharyngeal or bronchial irritation and restore comfort. These treatments may be given continuously with an electrically heated inhalator or at intervals of three hours while the patient is awake. When administered intermittently by a nurse, steam inhalations can be prepared by filling an earthenware pitcher halfway to the top with scalding water, adding a teaspoonful of compound tincture of benzoin, and wrapping a towel around the top of the pitcher in the form of a funnel or mask. The patient inhales the medicated steam as long as it is emitted from the pitcher, usually about ten minutes. Menthol is not very satisfactory as a medication, since it tends to induce lacrimation.

Since the chief benefit of a gargle lies in the application of moist heat (115 to 120° F.) directly to the affected surfaces, the type of medication used is of less importance than the frequency and duration of the treatment. A simple normal salt solution gargle is probably as effective as any of the more highly flavored and complicated medications. A soothing and effective gargle can be compounded by dissolving 1 teaspoonful each of salt, soda, sugar, and borax in 1 quart of warm water. Gargles or throat irrigations should be taken every hour or two during the day. Local applications to the tonsils and pharynx of antiseptics, such as silver nitrate solution (2 per cent) or Scott's solution, probably do neither good nor harm, but they are much appreciated by some patients.

The presence of unusual reddening of the pharynx or of a marked systemic reaction should suggest the advisability of securing a throat culture. If the infection is streptococcal in nature, it will usually yield readily to sulfadiazine or penicillin therapy. No matter what the local or systemic treatment may be, the proper treatment of respiratory tract infections demands the maintenance of an adequate fluid intake; the patient should take an average of at least 200 c.c. of fluid by mouth every hour when awake.

### Bronchitis

If postoperative tracheobronchitis develops, the patient's chest is examined at frequent intervals to detect any evidence of an incipient atelectasis or bronchopneumonia. Steam inhalations, preferably constant, are of some value in helping to liquefy the exudate in such cases. When the cough is irritative and nonproductive in type, codeine alone or in a sedative cough mixture will prove most useful, but in the treatment of bronchitis characterized by the usual thick viscid exudate, an expectorant drug such as ammonium chloride, guaiacol, or sodium iodide is more suitable.

Epinephrine (0.5 c.c. of 0.1 per cent solution hypodermically) may be employed if there appears to be an asthmatic component of the bronchitis and if there is no systemic contraindication. Epinephrine also may be given by direct inhalation as a fine mist blown into the mouth from a glass nebulizer. The tiny droplets of epinephrine solution act directly upon the bronchial walls, through which they are absorbed within a few seconds after inhalation. For administration in this manner, epinephrine is used in 1.0 per cent (1:100) solution, which is too concentrated for use by injection. This treatment is most effective in mild asthmatic attacks and should be instituted when symptoms first appear. As a rule, asthma is relieved before enough epinephrine is absorbed into the circulation to cause systemic effects. For more severe asthma, aminophylline, 0.24 Gm. (gr.  $3\frac{3}{4}$ ), may be given slowly intravenously with good effect. Morphine is not used in asthma; besides the possibility of inducing habituation, morphine may increase the bronchiolar constriction and depress the respiratory center.

The administration of sulfonamides or penicillin in therapeutic dosage may be advisable both to combat the infection and to prevent the development of pneumonitis.

The patient, who has little appetite as a rule, will prefer a liquid or soft diet to a full one during this period. Elevation of the head of the bed generally increases the ease of respiration and tends to reduce the irritative effect of the bronchitis. Proper ventilation of the room must be secured but direct drafts should be avoided; room temperature is maintained within a range of 70 to 80° F.

### Persistent Vomiting

When postanesthetic nausea and vomiting are prolonged, the patient may be induced to swallow rapidly two full glasses of lukewarm water, with or without added salt or sodium bicarbonate. The fluid is immediately regurgitated and consequently acts as a lavage, carrying along the irritative stomach contents. Sometimes, in case of persistent nausea, the patient may ask for certain types of fluid or food; these are usually safe to give and may be followed by cessation of vomiting. Nausea may respond also to the administration of small amounts of carbonated drinks, such as ginger ale or Coca-Cola, or to a small dose of spirit of peppermint (U. S. P.) given in a dose of 1 c. c. in water or on a lump of sugar. Sedative or antispasmodic drugs, given hypodermically, are often effective (p. 120).

As a result of continued vomiting, loss of fluids, and consequent starvation, the patient may develop acidosis, evidenced clinically by the manifestations of dehydration, by the presence of ketone bodies in the urine, and by a decrease in the carbon-dioxide combining power of the blood. Corrective treatment, by intravenous administration of normal salt and dextrose (5 per cent) solutions, must not be delayed until signs of physiologic disturbances appear but must be instituted as soon as the vomiting is noted to be more than ordinarily severe.

Although restoration of the depleted body fluids and electrolytes usually is sufficient to stop prolonged vomiting, gastric lavage usually is necessary. This treatment, when indicated, should be performed before the patient has become weakened. Protracted retching, especially if the stomach is empty, may produce slight gastric hemorrhages from rupture of small mucosal blood vessels. If intravenous fluid is to be given as a therapeutic adjunct to gastric lavage, it should be administered following the introduction of the stomach tube, so that the severe straining that usually accompanies passage of a catheter down the esophagus will take place before the patient's blood volume and consequently the blood pressure have been raised by the injection of fluids into the blood stream.

Passage of a stomach tube is an unpleasant experience for any patient and the purpose and method of the procedure should be explained to him. The most widely used type for

postoperative gastric lavage or decompression is the Levin catheter, a small tube which is introduced through the nose and may be maintained in position as long as necessary. To prevent soiling of bedclothes, a rubber apron or sheet is spread over the patient's chest and the part of the bed likely to become contaminated. If a dose of morphine sulfate, 10 to 16 mg. (gr. 1/6 to 1/4), or of some similar sedative drug is given hypodermically thirty minutes before introduction of the tube, the procedure is less likely to be troublesome.

The patient is propped up, if possible, in a semisitting position to facilitate swallowing of the tube. The catheter is kept coiled in a basin of ice water until the patient has been prepared; the tip is then lubricated with oil or glycerin and inserted into the patient's nose. It must be remembered that the direction of the nasal cavity does not extend upward but is approximately horizontal; the tube is consequently passed directly backward. When the tip reaches the posterior pharyngeal wall, it is pushed a little farther and the patient is instructed to swallow. Frequently at this point the distressed subject will attempt to seize the tube or will regurgitate the tip so that it presents at his mouth. Cooperation must be obtained by gentleness and persuasion; the patient is instructed to stop swallowing when he feels a wave of nausea approaching and to breathe deeply for a few seconds. When the sensation has entirely passed, several more swallows, aided by light pressure on the tube by the physician, will assure its passage into the stomach. The swallowing of several mouthfuls of water may help. The tube is then taped to the upper lip and to the cheek. There is no likelihood that a stomach tube will be passed into the trachea unless the patient is unconscious; it is preferable not to pass a stomach tube on an unconscious patient unless the glottis is visualized with a laryngoscope.

Lavage may be carried out by means of a syringe of 30 to 50 c.c. capacity, the process being repeated until the washings return clear. The tube is likely to become clogged with mucus frequently in some cases. Several hundred cubic centimeters of sodium bicarbonate solution (2 per cent) then may be introduced into the stomach and further attempts at lavage made after a short interval. Inability to recover lavage fluid that has been injected into the stomach sometimes indicates that

the tip of the tube has either coiled up near the anterior wall or has passed into the duodenum. Withdrawal of the tube for a distance of several centimeters may place the tip in a

Suction apparatus used in certain cases of intestinal obstruction  
*University Hospital University of Minnesota*

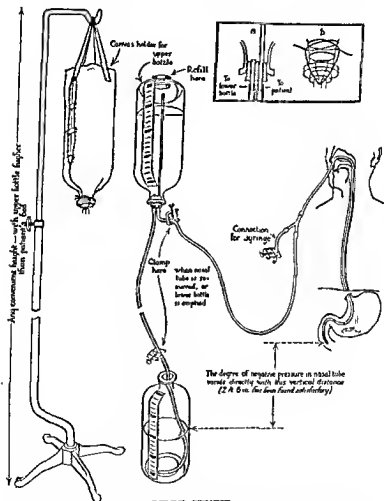


Fig 17—Apparatus for gastroduodenal suction. The upper bottle is hung from a standard by means of a canvas sling and the lower bottle is placed on the floor. If a Y connection is interposed between the nasal tube and the suction apparatus the tube can be aspirated and irrigated without disconnection of the suction. (From Wangenstein and Palou: *J.A.M.A.* 101: 1538, 1933)

more favorable position. The Levin tube, after insertion, may be left hanging over the bedside, attached to a drainage bottle for a few hours. Aspiration is attempted every hour or two by an attendant.

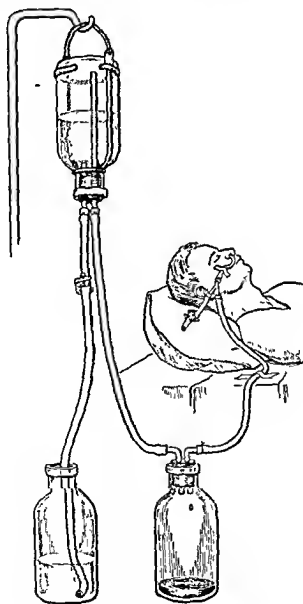


Fig. 18 —Gastroduodenal suction, Wangensteen method      Gastric drainage is  
"diverted into a collecting bottle"



When prolonged vomiting or intestinal distention is anticipated, a suction apparatus is used (Figs 17 and 18). This device, advocated and popularized by Wangensteen and Paine,<sup>1</sup> keeps the stomach and duodenum constantly empty by means of continuous siphonage. Use of this apparatus drains the secretions which accumulate during the period of postoperative intestinal atony but permits normal flow and reabsorption of gastrointestinal secretions after peristaltic activity returns. The amount of fluid recovered from the stomach is measured and charted daily and is entered into the calculation of total fluid intake required each day (p. 30). Sufficient fluids are supplied intravenously to insure a urinary output of 1,000 to 1,500 c.c. daily and to maintain the blood electrolytes at their proper levels. Although this apparatus is useful in the management of protracted vomiting, its greatest value is in the prophylactic treatment of those patients in whom the development of postoperative adhesions, intestinal obstruction, or gastric dilatation is feared.

### Intestinal Distention

Operations in which the peritoneal cavity is entered are practically always followed by a variable degree of intestinal paresis, generally considered to result from the unavoidable handling of the intestine and traction on the mesentery during operation. Excessive stimulation of the vegetative nervous centers of the abdomen, in operations upon the kidney as well as within the peritoneal cavity, and trauma to the intestinal wall produce relaxation of the intestinal musculature. Tension within the lumen of the bowel is consequently reduced and the contained gas, unopposed by the normal muscular tonus of the bowel wall, causes a generalized ballooning of the small intestine. Other factors contributing to intestinal distention include swallowing of air during induction of and recovery from anesthesia, swallowing of air by the nauseated patient in efforts to reduce his nausea, transudation of gases from the blood stream into the lumen of the atonic bowel, and perhaps fermentation by the bacterial flora of the bowel of such ingested material as milk and sweetened fruit juices. There is some doubt whether the factor of fermentation plays much part in contributing to intestinal distention.

Nonabsorbable gases from these sources remain in the distended bowel until the parietic intestinal wall has regained its tonus and the ability to expel its contents, which usually occurs within forty-eight hours. The efforts of segments of the stretched bowel to force the gases along are probably responsible for the familiar gas pains. It is not, of course, necessary that the entire intestinal tract be distended with gas for the typical symptoms to develop; one or more segments of bowel may become temporarily impaired in motility as a result of operative handling and may obstruct the progress of normal peristaltic waves. Total disappearance of severe gas pains is often simultaneous with the passage of a relatively small amount of intestinal gas.

Since the factors responsible for intestinal distention are present during and after every intra-abdominal surgical operation, the control of distention begins with efforts to minimize the causative factors. Such measures include (1) preparation of the bowel before operation with low residue diet and enemas; (2) adequate preoperative sedation, with smooth and skillful induction of anesthesia to reduce excitement and air-swallowing to a minimum; (3) as little manipulation of the intestine as possible during operation; and (4) active prophylaxis in the early postoperative period by prompt treatment of nausea and vomiting and by proper regulation of the diet and fluid intake, with institution of light, solid diets as soon as possible and avoidance of slow-digesting foods. When disturbed function of the gastrointestinal tract is present before operation, or when operation upon the gastrointestinal or biliary tract is planned, it is advisable to insert a Levin tube before induction of anesthesia and to maintain suction during the course of the operation.

Although intestinal distention is a minor and frequent postoperative complication, it cannot be ignored or regarded lightly. Paralytic intestinal obstruction, always a dangerous development, may begin in the same way as a simple intestinal distention, and, like all other forms of intestinal obstruction, its mortality rises with delay in institution of treatment. Simple distention that does not respond to the ordinary therapeutic measures must be considered to be paralytic obstruction and treated accordingly. Intractable intestinal distention, in fact, may foreshadow the development of true paralytic intestinal

obstruction, one condition merging gradually into the other with no well-marked definitive changes

As a rule, attempts to stimulate the relaxed gut are of little avail for the first two or three days, after which time tonus returns spontaneously and motility soon may be restored to normal. Simple passage of a well-lubricated rectal tube may be sufficient to remove the gas that a painful abdominal wall cannot aid in pushing past a spastic sphincter. The tube may be inserted at intervals of two to four hours during the first three days while the patient is awake and allowed to remain in place for perhaps half an hour each time. This procedure is frequently used as a prophylactic measure to avoid development of distention of the colon. If introduction of the tube alone is insufficient, a small irritant enema, such as water, 2 ounces, and glycerin, 2 ounces, with or without 1 ounce of hydrogen peroxide added, may produce the desired effect. If not contraindicated, a 500 c.c. soapsuds enema at 110° F or an enema of 100 c.c. each of milk and molasses may be effective. Any of these enemata, followed by the application of hot turpentine stupes to the abdomen, with a rectal tube allowed to remain in place during this time, will usually relieve even a stubborn case of paralytic post-operative distention. A heat tent over the abdomen sometimes is used as an adjunct to other forms of treatment.

If it is certain that no mechanical obstruction is present, various peristaltic stimulants can be used. Peristaltin, a cascara extract, is not of proved value. Physostigmine (eserine) is not regularly effective and is definitely contraindicated because of its side effects. Morphine, formerly believed to cause intestinal atony, actually produces increased tone of the small bowel and relaxation of the large intestine, so that gas and intestinal contents tend to accumulate in the colon following the use of opiates. Pitressin, the pressor fraction of posterior pituitary extract, is probably more effective than whole pituitrin and is administered intramuscularly in 10 unit doses. This drug is a powerful stimulant to the colon and, conversely, appears to relax the musculature of the small bowel. One dose is often sufficient; if not, a second dose may be given in two hours. A rectal tube should be inserted at the time the drug is given, since its action begins within two or three minutes and persists for one-half to one hour. If the second dose is ineffective also, further doses are

useless. Pitressin, in conjunction with enemas, is most useful in the management of postoperative distention of the colon, which is found particularly following the repeated administration of morphine. The drug is a valuable therapeutic stimulant of colonic peristalsis, but it causes an appreciable rise in blood pressure. For this reason, repeated doses should not be used in patients who have hypertension or coronary arterial disease nor should Pitressin ever be given intravenously.<sup>2</sup> In the management of intestinal distention following the use of morphine in patients of this type, the frequent introduction of a rectal tube and the administration of small enemas usually will be sufficient.

Prostigmin acts in much the same manner as morphine, producing increased peristalsis in the small bowel and decreased contractions in the colon. Use of this drug therefore is best adapted to the management of distention and intestinal atony due to handling of the small bowel. The intestinal contents which tend to accumulate in the colon should be evacuated by means of enemas, particularly if morphine is used for the systemic relief of pain.

Some investigators feel that if a drug such as Prostigmin (1:4,000) is administered to the patient both before and after operation, the bowel never develops the temporary paralysis which gives rise to distention with its concomitant gas pains. Although many series of cases, such as those cited below, have been followed, with adequate controls, the evidence is still not sufficient to establish the value of such a procedure as a routine measure.

Marden and Williamson<sup>7</sup> report excellent results in forestalling postoperative atony of both the intestine and the bladder by use of a course of Prostigmin (1 c.c. of 1:2,000 solution) injections. Three single injections are given over the eighteen-hour period preceding operation and one injection every four hours after operation for four to six or more doses. No ill effects were observed by these authors, either on the vascular system or on the operative area, even following intestinal anastomoses. The reduction in incidence of gas pains and urinary retention was considered to be so marked in this group of patients that the procedure is advocated as a routine measure. Adams<sup>4</sup> cautions against the use of the more powerful peristaltic stimu-

lants such as Pitressin in cases of advanced intestinal obstruction, in which the muscular contractions may cause perforation of the overstretched, anemic bowel wall. This author states, however, that Pitressin is useful as a prophylactic measure and in early paralytic obstruction.

Hypertonic sodium chloride solutions may be tried in the treatment of postoperative intestinal distention, a dose of 20 c.c. of 10 per cent salt solution being given intravenously very slowly with a small needle. Stimulation of intestinal peristalsis and passage of flatus will occur within a few minutes if the treatment succeeds. If 5 per cent salt solution is used, doses of 50 to 100 c.c. are given. The amount of salt injected must be charted in the daily computation of salt and fluid intake. Use of hypertonic salt solutions is only occasionally effective in the treatment of intestinal atony and is likely to produce phlebitis at the site of injection.

If all these measures prove unsuccessful in the relief of the distention, an incipient mechanical or paralytic obstruction should be suspected and appropriate measures taken.

### Urinary Retention

The inability of the surgical patient to void during the early postoperative period is one of the most frequent and annoying problems of convalescence. Several causative factors are involved. Even a normal healthy individual has difficulty in voiding while in bed, particularly in the recumbent position, and for a patient just recovering from anesthesia and operation it is a far more difficult accomplishment. The remaining effects of the anesthetic interfere with bladder sensation as well as with ability to urinate, especially if spinal anesthesia or Avertin has been used. Narcotic drugs, of which morphine is one of the commonest offenders, reduce the sensation of bladder distention and increase the tonus of the sphincter musculature. Voluntary use of the abdominal muscles to initiate voiding is painful following operations upon the abdominal or pelvic viscera, and the effort may be too difficult for the patient. The bladder is displaced anatomically by most gynecologic operations as well as by operations upon the pelvic colon or rectum, and innervation of the musculature is disturbed at least temporarily in

most patients following these procedures. Also, a low-grade obstruction present in the lower urinary tract in a middle-aged or older male patient will interfere with normal voiding when other contributory factors such as the above are present, even though no symptoms of obstruction had appeared previous to confinement to bed and to operation.

Certain prophylactic measures may be taken before the problem of urinary retention arises. Since some people experience considerable difficulty in voiding while recumbent, the surgical patient may be given an opportunity to become familiar with the use of the bedpan or urinal during the preoperative period. The patient is required to void or is catheterized before going to the operating room. A useful method to reduce the incidence of postoperative urinary retention is the instillation of a mildly irritating antiseptic solution into the urinary bladder at the time of operation. It is a routine procedure in the gynecologic service of the Johns Hopkins Hospital to instill 1 ounce of Mercurochrome (0.5 per cent solution) into the patient's bladder by the usual sterile technique immediately following the completion of operation. Woodruff and TeLinde<sup>3</sup> report that by means of this simple measure the number of major gynecologic operative patients requiring catheterization has been reduced from 50 per cent to less than 7 per cent. Incidentally, the routine procedure includes, at the same time, the rectal administration of 1 liter of warm sodium bicarbonate solution (2 per cent) and 2 ounces of mineral oil to supply fluid and to render subsequent passage of feces easier.

The fluid intake during the first day after operation is more or less inadequate in the patient who receives no parenteral fluids, and large quantities of fluid are lost by routes other than the kidneys. For these reasons the amount of urine secreted during the first few hours after operation is not, as a rule, very great. The average patient will void from 200 to 400 c.c. of urine within six to eight hours after operation; if not, he should be examined for evidence of urinary retention. While sometimes visible and palpable, a full bladder almost always can be identified by percussion, a note of absolute flatness frequently extending halfway up to the umbilicus. Pressure upon the suprapubic area will produce discomfort and an intensified desire to void under these circumstances. The diagnosis can be confirmed

without difficulty by rectal or vaginal examination. A bladder that is demonstrable above the symphysis pubis by either palpation or percussion generally contains at least 500 c.c. of urine.

Close watch must be kept upon the total urinary output even though the patient does not complain of bladder distention. A patient who receives the usual fluid intake of 2,500 to 3,500 c.c. daily to maintain a normal fluid and electrolyte balance will excrete up to 1,500 c.c. of urine daily. An infusion, particularly if administered rapidly, will produce a diuretic effect, with the excretion of from 300 to 600 c.c. of urine within the next hour or two. Because of the decreased vesical sensation and reflexes in the early postoperative period, the bladder may become markedly overfull without producing the usual sensation of urgency. The patient, however, sometimes will be restless and in great discomfort without any localizing symptoms other than constant lower abdominal pain.

During the first day or two after operation the quantity of urine voided on each occasion must be measured or estimated by the nurse and noted on the patient's chart. If the total output seems small or if no urine is voided within six hours after operation, examination of the bladder region by the physician is indicated. Occasionally a patient will void very frequently in small amounts, perhaps 50 to 100 c.c. every hour or two, and may complain of lower abdominal discomfort. Voiding of this type usually indicates overflow incontinence, a state in which the overdistended bladder forces enough urine past the spastic sphincter at intervals to ease the tension temporarily. Well over a liter of urine may be present in the bladder in such a case.

It is unwise to allow the urinary bladder to become overdistended after an operation; severe stretching of the vesical wall may induce atony and interfere with later resumption of normal tone and also may impair the mural circulation to such an extent that mucosal edema and petechial hemorrhages will follow rapid decompression by a *too-long-delayed catheterization*. Such a condition is likely to interfere temporarily with the ability of the bladder to empty itself completely when contractility begins to return. The residual urine then serves as a culture medium for bacteria introduced by the catheter and the damaged mucosa may show an increased susceptibility to inflammatory changes.

Since a healthy bladder mucosa is highly resistant to infection, cystitis ordinarily does not follow catheterization properly performed before marked overdistention occurs.

Catheterization usually is necessary for urinary retention following an extensive surgical procedure, but simpler measures may be successful in a patient who is less severely ill. Frequently effective methods of inducing a patient to void include the administration of a small enema containing 60 c.c. each of water and of glycerin, administration of a small soapsuds enema (500 c.c.), and application of a lightly wrapped hot-water bag or of hot (115° F.) irrigations to the perineum when possible. Addition of 30 c.c. of hydrogen peroxide to the previously mentioned enemas sometimes increases their effectiveness. Use of parasympathetic stimulant drugs has been advocated, particularly derivatives of acetylcholine, which act with especial effect on the lumbosacral centers. Mecholyl (acetyl-beta-methylcholine), administered by mouth in a dose of 25 to 50 mg., is often of definite value. This drug should not be given hypodermically or intravenously for treatment of urinary retention nor should it be given by any route to patients in the older age groups, patients who are subject to asthmatic attacks, or patients with heart disease of any type or degree. Its use may be followed by systemic symptoms such as flushing, sweating, salivation, and a sensation of substernal tightness. Nausea and vomiting are evidences of toxicity and are not likely to occur with relatively small oral doses of the drug.

The use of Prostigmin has become widely popular as a routine measure for prevention of postoperative disturbances of micturition as well as for intestinal distention; it is administered in doses of 1 c.c. of the 1:4,000 solution hypodermically every two hours for six doses immediately preceding operation and for from two to six doses immediately after operation. Fully developed urinary retention may respond to a single injection of 1 c.c. of Prostigmin (1:2,000), repeated in two hours if necessary.

The presence of a drain in the space of Retzius or in the cul-de-sac or rectum will decrease the capacity of the bladder by reducing its room for expansion. When the drain is shortened or removed, difficulties in urinary evacuation usually disappear.

Patients who are not severely ill may be able to void if they are propped up in high Fowler's position or are allowed to sit



upright in bed. Following relatively minor operations, patients of either sex can be allowed to use a bedside commode if necessary. Although the exertion involved in such a procedure is a disadvantage, it is preferable to the possible establishment of a urinary tract infection following catheterization. Most surgeons have no objection to allowing patients to get up to void immediately after an operation such as an appendectomy through a muscle-splitting incision but prefer catheterization to allowing their arising immediately after other types of abdominal incisions. Advocates of routine early ambulation, however, maintain that normal urination and avoidance of catheterization are among the benefits and advantages of this measure.

Two of the most obvious and yet most frequently overlooked reasons for postoperative urinary retention are lack of privacy and lack of confidence. Initiation of micturition is hindered to a variable but sometimes an extreme degree even in normal healthy individuals by the presence of other people. Very often, a patient unable to void following operation may be able to do so if helped to a bedpan and then allowed to try by himself without the encouraging but distracting ministrations of an attendant. In other cases, lack of confidence follows one or two unsuccessful attempts to void and all measures short of catheterization then fail. Occasionally a patient will go through ten days to two weeks of convalescence before the ability to void normally returns. McLaughlin and Brown,<sup>9</sup> after investigating the problem of urinary retention in healthy young men subjected to various surgical operations, concluded that the commonest cause of postoperative inability to void is on a psychic basis and that proper nursing care and encouragement are the most effective answers to the problem. This investigator found that while Prostigmin in full dosage was effective in prevention of postoperative urinary retention, the results were fully as good when sterile normal salt solution was substituted for Prostigmin without the knowledge of the attendants or the patient.

When voiding cannot be induced by measures such as those mentioned, catheterization will be required and should not be deferred too long. Prolonged overdistention of the bladder will interfere with the return to normal tonus and encourage the retention of a residual quantity of urine. The resulting stag-

nation is the chief factor in the development of cystitis following catheterization, particularly if catheterization is repeated at long intervals. The procedure must be performed with strict adherence to sterile technique and an instillation of 1 ounce of a mild antiseptic is made before the catheter is withdrawn. Solutions frequently used include silver nitrate (0.1 per cent), Mercurochrome (0.5 per cent), boric acid (2 per cent), or aqueous Merthiolate (0.1 per cent). If the bladder has been allowed to become overfull, it is probably wiser to remove perhaps 400 c.c. of urine every hour or two until emptying is complete and the stretched edematous bladder wall has become accommodated gradually to the decreasing tension.

An order to catheterize the patient every eight hours if necessary is left as a routine in many cases. Such an order does not cover the possibility that bladder distention may develop rapidly and perhaps asymptotically if large quantities of fluids are given. It also places the responsibility for the decision upon an attendant who may not be aware that frequent voiding of small quantities of urine is an indication of overflow incontinence. Furthermore, in many cases the possibility of urinary retention is not even considered until the patient begins to complain spontaneously, by which time overdilatation may be severe. In every case, the surgical patient should be examined and his chart checked at least every six hours after operation to note if voiding in proper amounts has occurred. Catheterization should be repeated if necessary without regard for a fixed time interval, although no postoperative patient should be allowed to go more than eight hours without emptying his bladder, particularly after a catheter has once been inserted.

After the ability to void voluntarily returns, the presence of residual urine should be determined by catheterization immediately after voiding. Little or no urine should be obtained. If the quantity of residual urine exceeds 50 c.c., the patient should be catheterized in the same way routinely every six to eight hours immediately after each voiding until the residual amount on two successive catheterizations is less than 50 cubic centimeters. Retention of this puddle of contaminated urine in the bladder encourages the development of infection.

When the patient requires catheterization more than three successive times or when a significant residual urine persists,

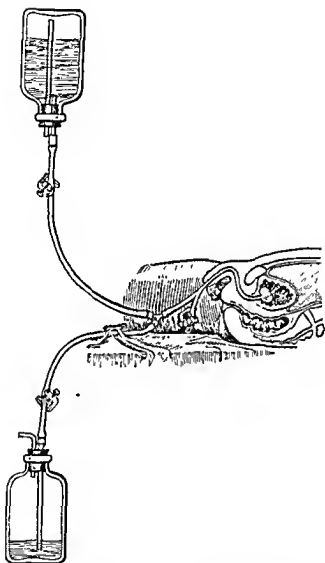
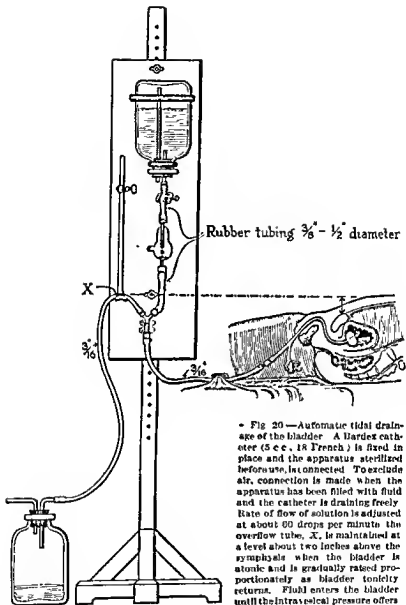


Fig. 10.—Urethral retention catheter. The catheter (Bardex type) is taped in place and is attached by means of a Y tube to a drainage bottle on the floor and to an elevated irrigating bottle containing a mild antiseptic solution. Irrigation is performed at occasional intervals as necessary.

the introduction of a urethral retention catheter is preferable to repeated catheterization. The catheter may be allowed simply to drain into a bedside bottle or may be attached by means of an extension and a glass Y tube to an infusion bottle containing a mild antiseptic solution (boric acid 2 per cent) and to a tube draining into an empty bottle on the floor (Fig. 19). All parts of the apparatus as well as the solution must be sterile. The bladder is kept empty by the drainage tube and the irrigating solution is used to wash out the bladder three or four times a day, quantities of 200 to 250 c.c. being used for each irrigation. This procedure prevents accumulation of residual urine, avoids the need for repeated catheterization, and minimizes the likelihood of introduction of bacteria into the bladder. The catheter is allowed to remain in place for at least several days, until the patient is active in bed and is in good general condition. Following withdrawal of the catheter, a test is made for residual urine as before. If persistent residual urine is still present, drainage is again instituted for a second period of one or two days. Presence of residual urine or of urination difficulties following a second period of drainage is an indication for cystoscopic investigation. The commonest cause of such prolonged retention in older men is previously asymptomatic slight hypertrophy of the prostate gland or of the detrusor muscle.

Although infection does not commonly develop in a properly drained or emptied urinary bladder, prophylactic doses of sulfadiazine should be given during repeated catheterization or use of a retention catheter. Full dosage is not necessary; a concentration of the drug in the urine sufficient for bacteriostasis can be attained by administration of 0.5 Gm. (gr.  $7\frac{1}{2}$ ) of sulfadiazine every four to six hours during the day and night. Sodium bicarbonate is given in twice this dosage and large quantities of fluids are administered to prevent crystalluria. Urine output is charted and the total output maintained between 1,000 and 1,500 c.c. daily. A diminished urinary output favors the development of bladder infection in these circumstances.



• Fig 20—Automatic tidal drainage of the bladder. A Hardex catheter (5 c.c., 18 French) is fixed in place and the apparatus sterilized before use. To exclude air, connection is made when the apparatus has been filled with fluid and the catheter is draining freely. Rate of flow of solution is adjusted at about 60 drops per minute. The overflow tube, X, is maintained at a level about two inches above the symphysis when the bladder is atonic and is gradually raised proportionately as bladder tonicity returns. Fluid enters the bladder until the intravesical pressure offers enough resistance to permit passage

of fluid along the overflow tube, X. Siphon drainage results and continues until the bladder is empty and air is drawn into the system, breaking the siphonage. The process then repeats itself, filling and emptying of the bladder continuing automatically. The air vent in the drip tube must be kept patent and the fluid reservoir must not be allowed to run dry. Sterile normal salt solution, phosphoric acid (0.25 per cent) solution, boric acid (1.5 per cent), or acriflavine (1:8,000) may be used for irrigating solutions. This apparatus is used when residual urine is high and return of normal micturition is slow, as in the case of the neurogenic bladder or in preoperative preparation for prostatic surgery when residual urine exceeds 100 cubic centimeters (Courtesy Dr. Paul L. Getroff)

## Urinary Tract Infection

Urinary tract infection may develop as a complication following almost any type of operation and usually is secondary to postoperative urinary retention with incomplete emptying and residual urine.

**Prophylactic measures** against infection must be taken following every catheterization (p. 333) and retention of residual urine prevented. Although frequent catheterization is certainly undesirable, potentially infected urine should not be permitted to stagnate in a bladder that has become atonic following overdistention. Frequently repeated catheterization or drainage by a retention catheter is imperative in such a case.

Certain patients are especially liable to development of residual urine and consequently have a tendency to develop bladder or kidney infections, for example, patients suffering from a chronic debilitating disease, patients confined to bed for long periods, patients with previous urinary tract disease, or people past middle age. Operations upon the pelvic organs in either men or women are often followed by urinary tract infections, as are operations of any type upon men with slight prostatic enlargement or women with cystocele or uterine prolapse.

**Symptoms** of urinary tract infection are often general; in many cases the onset is marked abruptly by chills, fever (temperature 101 to 103° F.), malaise, anorexia, and sometimes nausea and vomiting. Leucocytes are elevated, with a predominance of neutrophilic forms. Because of the lack of localizing symptoms, the condition is often erroneously diagnosed as gripe or "intestinal influenza" and the true nature of the disease may remain unsuspected until symptoms of cystitis appear. A specimen of urine, preferably catheterized in the female patient, therefore must be examined as a routine in the diagnostic differentiation of any obscure febrile postoperative complication.

**Local inflammatory symptoms** are confined to the bladder unless overdistention of the kidney pelvis occurs, with pain and tenderness in the costovertebral angle. A sterile specimen of urine should be secured, always by catheterization in the female

patient, for culture and microscopic examination. An occasional pus cell is without significance; acute urinary tract infection generally produces definite pyuria and many large clumps of pus cells will be seen. If the urine contains no pus and yet the symptoms clearly indicate the presence of urinary tract infection, ureteral obstruction may be present, with retention of infected urine in the kidney pelvis.

Acute infections of the urinary tract require immediate energetic treatment; persistence of the condition may result in a chronic infection that will be difficult to eradicate. Chemotherapy usually is effective within three to five days; if the infection has not shown a satisfactory response to treatment within this time, the advice of a urologist should be sought. At times these infections will require instrumental drainage; for example, if ureteral obstruction has developed.

Treatment is instituted promptly. Since the choice of therapy depends in part upon the type of organism causing the infection, a sterile specimen of urine must be secured for culture before treatment is begun. Cultures are taken subsequently at intervals of two or three days to determine any change in the type of bacteria present, so that the therapeutic attack may be altered accordingly.

Treatment of this condition has changed considerably in recent years. The introduction of penicillin and streptomycin and further experience with the sulfonamide drugs have made possible an amazingly prompt degree of control over most types of bacterial infections of the urinary system. These preparations have supplanted almost entirely the older remedies such as acriflavine, hexylresorcinol, sodium acid phosphate, and methenamine. Mandelic acid and the ketogenic diet occasionally are of value, especially in chronic infections, but are not used as a rule until chemotherapy has failed.

Sulfadiazine is perhaps the most useful of the sulfonamide drugs for treatment of mixed infections of the urinary tract. While it is most effective against streptococci, sulfadiazine also exerts some effect in staphylococcic infections. It is of less value in chronic infections and of almost no value against gram-negative bacilli. Full dosage of sulfadiazine is not necessary; an initial dose of 2.0 Gm. (gr. 30) may be given, followed by

0.75 to 1.0 Gm. (gr. 12 to 15) every six hours, together with double this dosage of sodium bicarbonate. The dosage for children is from one-half to two-thirds of the full dosage, calculated according to weight or age. Sulfadiazine is excreted at a fairly slow rate and is one of the least toxic of the sulfonamide drugs. Although serious toxic reactions rarely occur (p. 291), the chief disadvantage of the drug is that in occasional cases acetylsulfadiazine crystals will precipitate in acid urine, causing oliguria or even anuria due to kidney damage or ureteral obstruction. It is necessary therefore to maintain the urinary reaction at least close to the point of neutrality by administration of sodium bicarbonate or sodium *r*-lactate to minimize precipitation of crystals, even though alkalinity of the urine is more favorable to bacterial growth. While oliguria or anuria from this cause is unusual, particularly with the relatively small dosage of sulfadiazine required for control of urinary tract infection, the possibility must be remembered when the drug is used. Hematuria and oliguria occurring during administration of any sulfonamide drug are danger signals and require immediate cessation of its administration and prompt measures to improve the kidney function.

Simultaneous administration of sulfathiazole, sulfadiazine, and sulfamerazine in one-third dosage of each (p. 292) will secure full therapeutic effect with much less danger of crystalluria. Alkalinization of the urine is unnecessary when this combination of drugs is used in average dosage, although the fluid intake should be high.

Sulfacetimide is a very satisfactory drug for use in acute urinary tract infections due to gram-negative bacilli. Both the free and the acetylated forms are therapeutically effective and are highly soluble in acid or alkaline urine, and the drug exerts little or no toxic effect in therapeutic dosage. For treatment of mixed infections of the urinary tract, the administration of sulfadiazine or triple sulfonamides for a week will eradicate or at least control all the offending organisms except bacilli, which then may be cleared out successfully by administration of sulfacetimide. Sulfacetimide is given in doses of 1.0 Gm. (gr. 15) three or four times daily for three days, after which the dosage is reduced by half and continued for another week.



Penicillin is of great value in treatment of acute infections of the urinary tract due to gram-positive cocci and will often eliminate these organisms in mixed infections as well. It has no effect, however, upon gram-negative bacilli, nor is it of constant value in treatment of chronic infections of the urinary tract. A dosage of penicillin amounting to 20,000 units intramuscularly every two hours or 30,000 units every three hours should be used. The drug is excreted rapidly into the urine and produces a prompt effect in acute infections caused by penicillin-susceptible organisms.

Streptomycin is not a substitute for penicillin; it is effective only against gram-negative bacilli. In urinary tract infections due to *Escherichia coli*, *Proteus vulgaris*, *Aerobacter aerogenes*, or *Pseudomonas aeruginosa*, however, the rapidity and completeness of its therapeutic effect may be little short of amazing. Free drainage of the urinary tract is necessary; the presence of stones or of obstructions may render the drug entirely ineffective. Mixed infections do not respond well to streptomycin and prolonged administration or insufficient dosage is likely to increase the tolerance of the organisms to the drug so greatly that they will become completely resistant to streptomycin. After the organism responsible for the infection has been identified by culture, relatively large doses of streptomycin are administered from the beginning of treatment to clear the urinary tract of bacteria as quickly as possible. If a mixed infection is present, all the organisms resistant to streptomycin are cleared first by means of the appropriate drug, after which streptomycin is given in doses of 0.17 to 0.33 Gm. intramuscularly every four hours for five to eight days.

Chemotherapeutic and antibiotic drugs are most effective in acute infections; other forms of therapy may be required in treating chronic urinary tract infections.

Mandelic acid treatment was developed to replace the ketogenic diet, which is fairly effective but is difficult to administer and control properly. This therapy is of value in infections due to gram-negative bacilli, *Streptococcus fecalis* (enterococcus), and *Pseudomonas aeruginosa* but is not effective against *Proteus vulgaris*. It may be more effective than chemotherapeutic agents when residual urine is present. The preparations most commonly used include ammonium mandelate in aqueous

solution (10 per cent), elixir (20 to 30 per cent), or enteric-coated tablets. Calcium mandelate is sometimes preferred. Sufficient dosage is administered to supply a total of 12 to 16 Gm. of the drug a day, preferably divided into four doses of 3 to 4 Gm. each. Methenamine mandelate may be used in doses of 1.0 Gm. three or four times daily. Mandelic acid is effective only in an acid medium; the pH of urine must be maintained between 5.5 and 5.0, the reaction being checked by nitrazine test paper once or twice a day. The drug itself often suffices to acidify the urine to the proper degree; if not, ammonium chloride or ammonium nitrate may be given in addition. Total daily fluid intake is restricted to 1,500 c.c. to assure proper urinary acidification. The urine may become free of pus within four or five days after institution of treatment, but medication is continued for several days longer. Specimens of urine are secured under sterile precautions for culture three and six days after cessation of medication to establish the completeness of cure (Campbell').

Mandelic acid preparations sometimes produce gastric irritation; calcium mandelate or enteric-coated tablets of ammonium mandelate may be the most acceptable forms. Although the drug produces no toxic effects in therapeutic doses when kidney function is normal, it is not advised when renal disease is present, since under these circumstances it may produce renal irritation and will not be excreted in sufficient quantity to be effective.

Other drugs used frequently in infections of the urinary tract include methenamine and Pyridium. Methenamine is of value chiefly in bacterial infections and is effective only in acid urine, in which it liberates formaldehyde in small quantities. Methenamine is given orally in doses of 1.0 Gm. four times daily together with large quantities of water and sufficient amounts of ammonium chloride or acid sodium phosphate to maintain urinary acidity. Pyridium is of value chiefly for the relief of tenesmus, frequency, and bladder irritability caused by acute or chronic infection, although it exerts some bacteriostatic effect also. The drug is given in doses of 0.2 Gm. (gr. 3) three times daily before meals; it should not be used in the presence of renal damage or gastrointestinal tract disease.

Diet should be light and easily digested, containing a large proportion of carbohydrate. When chemotherapeutic or antibiotic drugs are being used, the fluid intake is increased to 3,000

c.c. daily to insure proper irrigation of the urinary tract. Fluids are restricted when the drug used is effective only in acid urine (for example, mandelic acid). Proper evacuation of the bowels is encouraged by administration of enemas or mild cathartics. Supportive measures in general are those indicated in the management of any acute febrile disease.

### Hiccough

Operations on the upper abdominal viscera are sometimes followed by hiccough. The mechanism of onset of the hiccough is not always clear; it may result from such widely divergent causes as peritonitis, or diaphragmatic irritation (as in pleurisy and subphrenic abscess), or dilatation of the stomach, or retention of toxic products in the blood (as in uremia). Merely an annoyance at the onset, persistent *singultus* may rapidly exhaust the patient's strength and produce marked depression or even death. Physiologically, hiccough is a sudden clonic twitch of one or both sides of the diaphragm, resulting in a sudden inspiration, interrupted by a reflex closure of the glottis. This spasmodic contraction is continued at intervals of a few seconds uninterruptedly and may interfere with sleep, speech, and the taking of food.

Medication usually has little effect, although a mild attack will sometimes respond to Hoffmann's anodyne (10 to 30 minims). Benzedrine (amphetamine sulfate) may be tried in doses of 5 to 10 milligrams. Some of the more time-honored remedies have apparently been empiric methods of increasing the blood carbon dioxide content; for example, holding the breath as long as possible or drinking a large glass of water very slowly. The most generally used treatment is administration of carbon dioxide by inhalation. When a gas machine is available, a single administration of 5 to 10 per cent carbon dioxide in oxygen for several minutes almost always will relieve the spasms if there is no physical basis such as an undiagnosed dilatation of the stomach. When no gas apparatus is obtainable, a simple but almost equally effective expedient is that of permitting the patient to rebreathe into a grocer's two-quart paper bag held tightly around the mouth and nose. If these measures are unsuccessful, gastric lavage should be performed; even though there is no actual indication,

the patient may have his attention so diverted by the procedure that the self-propagating rhythm of the hiccoughs may be permanently broken. A blood chemistry examination may reveal early nitrogen retention or evidence of early acidosis. When the deranged electrolyte balance or disturbed renal function has been corrected by appropriate intravenous fluids and other indicated therapy, the normal function of the diaphragm may be resumed.

In the most intractable cases, when thorough investigation reveals no abnormal conditions likely to produce hiccough and when all therapeutic procedures have failed, fluoroscopic examination should be done to determine which side of the diaphragm is producing the symptom. The phrenic nerve on that side is then anesthetized. Since the spasms often will disappear completely if their rhythm is interrupted for an hour or more, anesthetization of the nerve with procaine (1 per cent) is usually sufficient. The phrenic nerve is located too deeply to be reached effectively by simple injection; operative exposure of the nerve as it crosses the scalenus anticus muscle is the safest procedure and can be accomplished without difficulty under local anesthesia. Following injection of procaine into the nerve, a loop of silk thread may be passed beneath it and the ends of the loop brought out the incision. If the hiccough recurs after the procaine effect has disappeared, traction on the thread will control the spasm. In the most severe cases, temporary paralysis by crushing of one or even both phrenic nerves may be necessary.

### Skin

Patients who are debilitated because of age, malnutrition, metabolic disease, or neurologic or vascular lesions are particularly likely to develop pressure sores or decubitus ulcers when they are confined to bed. Constant and unaccustomed pressure upon the skin over bony protuberances, however, may produce painful irritation or necrosis and ulceration even in ordinary patients who have been subjected to severe operations and are undergoing prolonged convalescence. This complication, although usually more annoying than serious, may become in debilitated individuals the starting point for a spreading gangrene or extensive infection that may threaten life. Such an

occurrence in a diabetic patient may render dietary and insulin control of the metabolic disease all but impossible.

Since these lesions are the direct results of impaired circulation due to long-continued pressure upon areas in which bony parts lie close beneath the skin, prophylactic measures are of great importance. Patients in whom the development of decubitus ulceration is likely to occur should be allowed to lie upon a rubber ring to protect the sacrum or should be placed upon an air mattress. Frequent change of position is advisable to avoid prolonged pressure on any one spot, and evidences of skin irritation must be noted at once. Individuals with associated diabetes or arteriosclerosis must be watched with particular attention; ulceration over the sacrum or upon the heel may alter the prognosis completely.

The mildest forms of such skin lesions are usually manifested as reddened, dry areas over the sacrum, trochanter, heel, or olecranon and are painful, tender, and symmetrically distributed. The chief consideration is the relief of pressure upon the affected area; lesions on the sacrum are protected by placing the patient on a rubber ring or in the prone position, and lesions on the heels may be kept away from the bed by placing one or two pillows beneath the legs, just above the heels. While skin lesions resulting from irritation by the bedclothes are best managed by application of zinc oxide ointment and a soft dressing of silk, linen, or fine-mesh gauze, those resulting from prolonged pressure are best treated by measures designed to improve the local circulation and to toughen the skin. Alcohol (50 per cent) may be applied frequently during the day to such lesions if the skin is not broken, and the area dried and dusted with zinc oxide powder. Exposure of the involved area, especially if on the back, to infrared rays under the direction of a physiotherapist may be of value.

Actual decubitus ulceration or bedsore may develop with great rapidity once the affected skin is broken and may progress into large areas of persistent and spreading gangrene, without much evidence of purulent inflammation. Since the primary etiologic factor is the local impairment of circulation, one of the most important therapeutic measures is the relief of pressure. If the patient can be kept from resting his weight upon the lesion and if active measures to improve the general physical

condition are taken, the ulcerated area will often respond to simple cleanliness. Moist dressings are distinctly contraindicated; the tissues become edematous as a result, and the area of circulatory deficiency and gangrene spreads with increased rapidity. The ulcer should be kept dry; applications of gentian violet (1 per cent aqueous solution) may help to form a protective eschar and stimulate epithelization. Irradiation with infrared or ultraviolet rays, advocated by some, is less useful when topical applications of dyes have been made. When gangrene is extensive, scarlet red ointment (1 per cent), allantoin ointment (2 per cent), or nitrofurazone ointment may be of value.

It has been recognized for many years that there is a nutritional factor in the development of decubitus ulcers and that correction of anemia and of nutritional deficiencies is necessary to secure healing of the lesion. Mulholland and his group<sup>8</sup> have demonstrated the relation of hypoproteinemia to the occurrence of these lesions and the relation of dietotherapy to their correction. Investigations by these workers of the influence of diet on healing of decubitus ulcers in a small number of patients indicated that high caloric diets were ineffective until a high protein intake was added. Further conclusions drawn from these studies were that vitamin concentrates are ineffective unless adequate proteins are furnished and that moderate degrees of anemia do not interfere with healing when sufficient proteins and vitamins are supplied. In addition to local measures, therefore, proper treatment of decubitus ulceration should include correction of anemia by blood transfusion, of hypoproteinemia and malnutrition by increase in the protein content of the diet, and of subclinical avitaminosis by administration of therapeutic doses of the B complex vitamins and vitamin C. Intermediate high protein nourishments are of considerable value in replacing deficient protein.

Strikingly good results were obtained by surgical treatment of decubitus ulcers in paraplegic military patients during the final years of World War II. The excellence of the results can be explained partly by the fact that the patients in military hospitals were all young healthy men, but subsequent trials of the same procedure in ordinary hospital practice have produced equally prompt healing. Blood transfusions, high protein diet, high protein dietary supplements, and vitamin concentrates are

administered until the patient shows approximately normal hemoglobin, red cell, hematocrit, and plasma protein values. The ulcer is treated with dressings wet with penicillin solution (250 to 500 units per cubic centimeter) until infection is controlled, cellulitis has disappeared, soft necrotic areas have sloughed away, and granulations are clean. At this stage, fine-mesh dry gauze is applied to the lesion and is covered with a bulky pressure dressing, the entire dressing to be changed daily by aseptic technique. After several days of dry dressings, the edema consequent to wet dressings has subsided and the ulcer is ready for treatment. The ulcer may be excised, widely undermined, and closed<sup>14,15</sup> without tension by rotating flaps from above and below. If the patient is prepared properly and wide flaps are developed at operation to permit closure without tension, the results following closure are superior to those following skin graft. In either case prophylactic use of penicillin (25,000 units every three hours) or of sulfadiazine (1.0 Gm. every four hours) for several days is advisable.

In some patients, particularly obese individuals, a succession of small furuncles may develop over the shoulders and back or a large boil may appear on the buttocks or sacral region. Frequent applications of 50 per cent alcohol used from the first sign of onset will sometimes avert the spread or progression of this type of inflammation. Application of several coats of half-strength tincture of iodine to the incipient furuncles has been advocated. The patient should be kept from lying upon the area if possible, pillows being arranged around the shoulders or a rubber ring supplied for support of the buttocks. In the presence of a marked infection of this type it may help to place the individual on his side or abdomen, remove all covering over the involved area, and place a cradle or tent in the bed to support the weight of the bedclothes. Penicillin and sulfonamides are obviously of value in such cases.

Carbuncles, which are commoner in patients with diabetes, especially when obese, may be treated with hot wet dressings for a short time and then incised. A gridiron pattern of parallel incisions without subsequent packing, as advocated by Maes and Heringman,<sup>11</sup> is the simplest and most effective method of surgical treatment, resulting in rapid healing and epithelization. Any preparation applied locally to an infected area should be

colorless; dyes will mask the progression or recession of the inflammation. For this reason, gentian violet is not used, although it is perhaps of some value in treating staphylococcus infections elsewhere. Sulfathiazole in full dosage or combined sulfonamides (p. 292) may be administered orally, or penicillin may be given intramuscularly. Penicillin administered by injection into and around the area of infection is still on clinical trial and cannot be recommended generally.

Necrotic tissue accumulating in the cavity may be removed by irrigation with hydrogen peroxide and subsequent flushing with sterile normal salt solution. Chlorophyll or nitrofurazone may aid in cleaning necrotic tissue from granulating areas and in promoting a healthy response of new tissue. The ointment or solution is applied daily to the sloughing area and covered lightly with a soft gauze dressing. Packs are not used following incision of carbuncles, for they block drainage, increase irritation, and cause great pain during dressing.

If the skin around a developing carbuncle, especially in an obese diabetic patient, is soggy and infiltrated, wet dressings are contraindicated since they encourage edema, with further impairment of blood supply and spreading of virulent organisms over the surrounding skin. Dry radiant heat over the uncovered area can be supplied by an ordinary electric light or by occasional exposure to infrared or ultraviolet irradiation. The skin is kept soft by application of sterile petrolatum.

### References

1. Wangenstein, O. H., and Paine, J. R.: Treatment of Acute Intestinal Obstruction by Suction With a Duodenal Tube, *J. A. M. A.* 101: 1532, 1933.
2. Seed, L., Falls, F. H., and Fantus, B.: Pitressin (Beta-Hypophamine) in Laparotomies, *Surg., Gynec. & Obst.* 64: 895, 1937.
3. Marden, P. S., and Williamson, E. G.: Use of Prostigmine Methyl Sulfate in Prevention of Intestinal Atony and Urinary Bladder Retention, *Surg., Gynec. & Obst.* 69: 61, 1939.
4. Adams, H. D.: Clinical Value of Morphine and Pituitary Extract, Pitressin, in Abdominal Surgery, *S. Clin. North America* 17: 773, 1937.
5. Woodruff, J. D., and TeLinde, R. W.: Postoperative Care of the Urinary Bladder, *J. A. M. A.* 113: 1451, 1939.



6. McLaughlin, C. W., Jr., and Brown, J. R.: Postoperative Urinary Retention; Clinical Study of 1,964 Naval Recruits Subjected to General Surgical Procedures, U. S. Nav. M. Bull. 12: 1025, 1944.
7. Campbell, M. F.: Pathogenesis and Present Day Treatment of Urinary Infections, Bull. New York Acad. Med. 15: 609, 1939.
8. Mulholland, J. H., Co Tui, Wright, A. N., Vinci, V., and Shafiroff, B.: Protein Metabolism and Bed Sores, Ann. Surg. 118: 1015, 1943.
9. Croce, E. J., and Beskes, C. H. C.: The Operative Treatment of Decubitus Ulcer, New England J. Med. 237: 141, 1947.
10. Conway, H., Kraissl, C. J., Clifford, R. H., III, Gelb, J., Joseph, J. M., and Leveridge, L. M.: The Plastic Closure of Decubitus Ulcers in Patients With Paraplegia, Surg., Gynec. & Obst. 85: 321, 1947.
11. Maes, U., and Heringman, E. C.: Advantages of the Gridiron Incision in the Treatment of Carbuncles, Am. J. Surg. 72: 166, 1946.

## CHAPTER 13

### MAJOR POSTOPERATIVE COMPLICATIONS

The more serious complications of the postoperative period frequently begin as relatively minor disturbances, the importance of which may not be recognized at the time. Proper care and management of such untoward incidents in their early stages will often prevent them from progressing into more serious complications that may terminate fatally. Appearance of a bed sore or of a skin infection, for example, in a diabetic patient who is showing an uneventful convalescence will sometimes precipitate a metabolic disturbance that may prove all but uncontrollable. A good-risk patient may develop a tracheitis or a mild bronchitis following an ether anesthesia. Ordinarily easy to control, such an inflammation of the respiratory tract may promote the development of a massive collapse of the lung with subsequent pneumonic consolidation of variable degree, particularly if the respirations are kept depressed by too frequent doses of morphine or by fixation of the lower chest with adhesive strapping over an upper abdominal incision. Marked abdominal distention may precipitate anginal attacks in a susceptible person, and a possibly fatal dilatation of the stomach may develop for want of a properly timed gastric lavage.

Very frequently a serious or fatal complication of the postoperative period can be traced back in this way to a seemingly minor disturbance, harmless in itself but responsible for the initiation of a chain of events that culminates in a condition threatening the life of the individual. Physiologic deficiencies and potentially dangerous infections present before operation must be sought and corrected; those developing after operation must be recognized and attacked in their incipient stages or, better still, foreseen and prevented.

#### Postoperative Shock

Postoperative shock is easier to prevent than to treat. Correction of nutritional deficiencies and treatment of associated disease before operation, with avoidance of ill-considered pro-

cedures, will produce more improvement in operative mortality statistics than the most expert treatment of postoperative shock resulting from lack of proper preoperative preparation.

Recognition of fully developed peripheral circulatory collapse is simple, but therapy at this stage is not always effective. Shock must be noted in its early stages, which usually appear within the first twelve hours after operation; it should be suspected when the pulse becomes rapid and running and the blood pressure and pulse pressure begin to fall steadily. A hypertensive patient may exhibit the symptoms of early shock even though his blood pressure may have dropped only to a level approximating the average normal value, which would, however, represent a severe drop of pressure from a hypertensive level. Such premonitory signs of impending circulatory collapse require prompt and energetic treatment to forestall the development of clinical shock.

The immediate therapeutic measures must include not only restoration of the blood volume and control of the peripheral circulatory collapse, but also treatment of any associated contributory factors which may have been present before operation or may have developed later.

The patient who was admitted to the hospital in shock or who developed shock in the early postoperative period has an increased tendency to develop other complications as convalescence proceeds. A close watch should be kept during the following days for evidences of atelectasis, anemia, venous thrombosis, or wound complications.

### Hemorrhage After Operation

Hemorrhage after operation usually will produce typical signs, both local and general. If continued postoperative loss of blood is superimposed upon the postanesthetic recovery stage, diagnosis may be difficult, the signs often suggesting anesthetic and operative shock rather than simple hemorrhage. With concealed blood loss during the immediate postoperative period, the shocklike picture appears abruptly, even though the patient has apparently rallied following the operation, and steadily deepens, the pulse rate rising progressively and the blood pressure dropping. If the patient is conscious, the sensorium usually is dulled, although a moderate degree of anxiety and restlessness may be

exhibited. Thirst may be marked. While shock alone also produces a certain degree of pallor, the lack of color resulting from continued hemorrhage has a characteristic lividity that may render it distinguishable at a glance.

Symptoms and signs vary with the site of the hemorrhage. Loss of blood into the tissues is limited by the local capacity for distention, and the resulting swelling may be easily visible. Loss of blood into a body cavity usually can be diagnosed, but occasionally it may produce no localizing indications of any kind. Hemorrhage into the chest will produce the dyspnea and physical signs typical of fluid in the pleural space. Free hemorrhage into the abdominal cavity, often but not always productive of pain, may be diagnosed by the presence of an increasing area of dullness to percussion, usually in the flanks, which is rarely extensive enough to shift with a change in the patient's position. The diagnosis sometimes can be confirmed by the presence of a soft mass in the cul-de-sac evident on rectal or vaginal examination. Hemorrhage into the lumen of the bowel may reach almost fatal proportions before it is evacuated as a copious tarry stool and often can be diagnosed only by exclusion. A minimum of 100 c.c. of blood is required to produce a tarry stool. Such a hemorrhage should always be anticipated as a possible complication in patients who have ulcerative lesions of the gastrointestinal tract or a lesion causing obstruction of the portal vein.

If concealed bleeding is suspected, hourly pulse and blood pressure readings, hemoglobin determinations, and red blood cell counts should be taken. Shock or peripheral circulatory collapse is marked by hemoconcentration due to plasma loss, while continued hemorrhage, since blood cells are also withdrawn from the circulation, usually is followed by blood dilution. As a result of blood loss, tissue fluids pass into the blood vessels from the extravascular tissues to preserve the blood volume as well as possible, with a resulting relative decrease in the concentration of the cellular elements of the blood. Falling blood pressure, falling hemoglobin, rising pulse rate, and increasing pallor therefore are the most dependable signs of a progressing concealed hemorrhage. It must be emphasized, however, that an acute massive hemorrhage may cause collapse so rapidly that there may be no time for significant alterations to occur in the

concentration or relative proportions of the constituents of the blood

Whatever the location of the bleeding point, measures must be taken to stop the blood loss as quickly as possible. If it is a simple incisional hemorrhage, one or two deep sutures about the oozing vessel will suffice. A large hematoma deep in the wound, however, may necessitate return of the patient to the operating room, evacuation of the clot, and location of the point of hemorrhage. An incision which contains a massive blood clot heals very poorly and is highly susceptible to the development of infection. Slight bleeding within the abdomen or gastrointestinal tract may require no treatment except absolute rest and frequent administration of morphine to allay apprehension. Once it becomes apparent, however, that the blood loss is continuing, there should be no delay in reopening the incision in the operating room and controlling the hemorrhage. When introduction of sutures is difficult or impossible, the use of gelatin sponge and thrombin (topical) solution or of absorbable gauze (oxidized cellulose) will achieve prompt control of hemorrhage from almost any bleeding point that is accessible. If the continued bleeding is due to a hemorrhagic tendency such as thrombocytopenia, an immediate transfusion of fresh blood is indicated to supply the lacking factor until clotting can occur, while in the hypoprothrombinemia characteristic of jaundiced patients, specific therapy is required in addition.

The lost blood must be replaced by properly matched transfusions. These should be given very slowly to avoid the production of a rapid rise in blood pressure. Vasoconstrictor drugs also are dangerously likely to increase the blood pressure too suddenly and therefore may interfere with the formation of a clot at the bleeding point. Intravenous infusions of normal salt solution and dextrose or transfusions of plasma, administered slowly, will serve to maintain the blood volume and blood pressure for the time necessary to prepare a transfusion in treatment of massive hemorrhage. Introduction of these fluids may increase blood loss, however, if administered during the progress of the hemorrhage. Such treatment consequently should not be given until the blood loss has been controlled, unless shock is threatened.

After the bleeding vessel has been secured or the impossibility of controlling the hemorrhage by local measures has been established, the patient is placed horizontally or with his feet elevated and is covered with blankets. Morphine, 10 to 16 mg. (gr. 1/6 to 1/4), is given hypodermically and a transfusion of blood is administered very slowly. If the patient is in shock as a result of hemorrhage, supportive measures must be instituted before operation is undertaken. The procedure to be followed in each case is a matter for individual judgment. The effectiveness of indirectly transfused blood in increasing the coagulability of the recipient's blood is not altered by the added sodium citrate, since there is always sufficient excess calcium in the recipient's blood stream to combine with the anticoagulant.

If the hemorrhage has been a mild one, the patient usually will respond satisfactorily to the accepted treatment for secondary anemia. Since the hemoglobin reaches a stable level within four to six days after cessation of hemorrhage, the necessity for transfusion of blood in addition to administration of simple hematinics may be determined at that time.

### Septicemia

Septicemia may develop in any surgical patient with a pyogenic focus of infection that is insufficiently drained. It is frequently possible, however, to cultivate organisms from the blood stream of a patient with a large abscess or carbuncle with no clinical evidence of actual septicemia. The few bacteria that spread into the blood stream by lymphatic channels or by direct extension from an infected thrombus in a vein at the original focus are readily destroyed by the natural defenses and no spread of infection results. In other cases the patient's general condition may be so poor or the operative procedures may have caused such a lowered bodily resistance that the steady infiltration of small numbers of bacteria into the vascular channels may result finally in the establishment of metastatic foci of infection. Each focus then repeats the process of destruction found at the original site. Bacteremia in pyogenic infections usually indicates clinical septicemia, but small numbers of organisms may appear in the blood without necessarily producing secondary foci of infection.

As in all bacterial disease, the clinical picture and the course of the infection depend upon the type and virulence of the organism, the size of the infecting dose, the number and frequency of such doses, and the state of the individual's general health and specific resistance to the infecting organism. An overwhelming infection in a patient with little resistance may produce marked prostration, with a swinging type of fever, rapid running pulse, and all the evidences of severe toxemia. These patients, especially if aged or already weakened by an unrelated disease, usually succumb rapidly. In others the clinical course may be a slow one, with a gradual development, a relatively lengthy course, and a prolonged convalescence or steady decline. The most favorable type is that with a quick febrile response, a rapid overcoming of the infection, and a fairly speedy recovery.

Diagnosis is not usually difficult, although cultures of the blood may often prove negative. In patients in whom septicemia is suspected, an exhaustive search must be made for the primary focus, and daily blood cultures should be taken. Infected areas not noted or not properly treated before operation may be responsible; for example, dental abscesses, boils, infected tonsils, or abscessed ears. The white blood cell count usually is elevated to an exceedingly high degree, with a pronounced shift to the left in the Schilling hemogram, the increase in total count being due to a rise in the percentage of polymorphonuclear neutrophilic leucocytes. In patients who are succumbing to an overwhelming infection, the white cell count may drop to a low level, perhaps even below normal. This is an extremely bad prognostic sign and is usually terminal in occurrence. Temperature, pulse rate, and respiratory rate are altered more or less in conformity with the general type of clinical response, the severest infection usually producing the greatest toxicity. A swinging type of temperature curve is the most typical form. The organisms most often responsible for surgical septicemia are the hemolytic streptococcus and staphylococcus, and, less frequently, the nonhemolytic forms. *Escherichia coli* is also a frequent invader.

**Treatment.**—The most important single step in the treatment of septicemia is the location and proper drainage of the primary focus. If this is a superficial abscess, it should be widely incised. Exploration with the finger is not advocated; the well-

localized abscess wall may be broken down and the cellulitis allowed to spread. A diffuse cellulitis should never be incised; hot wet dressings must be used until localization occurs. Before the introduction of chemotherapeutic and antibiotic drugs, ligation of the regional draining vein in a normal area well beyond the zone of infection was advocated in suitable cases. While this is no longer necessary when the primary focus is a small one, it is a lifesaving procedure in treatment of massive infections. Lateral sinus thrombosis, for example, may require the ligation of the internal jugular vein, and puerperal septic thrombophlebitis of the uterine veins may require ligation of the inferior vena cava and the ovarian veins (p. 394).

Foci of infection within the body are sought and treated as indicated according to their location. Kidney infections, peritoneal pus pockets, and splenic abscesses are not too difficult to discover, but lung or liver abscesses may offer more of a problem in diagnosis. Subphrenic abscesses may be most puzzling of all and are sometimes almost indistinguishable from localized empyema or liver abscess. However, treatment of the systemic infection must be based on eradication of the original focus and prevention of the introduction of fresh bacteria into the blood stream. Unless such control of the primary site can be established quickly, metastatic abscesses may develop and render sterilization of the blood stream practically impossible.

Maintenance of the patient's general health is imperative. Fluid losses increase with the rise in temperature and must be counterbalanced by administration orally and parenterally of the proper amounts to make up for the loss. In patients suffering from long-standing infections, the consequent breakdown of body protein, malnutrition, and vitamin starvation assume great importance and require corrective therapy. In severe systemic infections, the daily loss of protein may amount to as much as 50 Gm., and serious wasting of body tissues promptly results. The patients have no inclination to take food and it is difficult to supply enough protein by diet even to satisfy the daily basal nitrogen requirement. It is in such cases as these that the parenteral use of protein hydrolysates is of the greatest benefit; nearly 100 Gm. of complete protein can be supplied daily by intravenous administration of 2,000 c.c. of protein hydrolysate solution (5 per cent) in divided doses, with or without added



dextrose (p. 76). Additional quantities of protein can be given in nutritional mixtures introduced by stomach tube or, in some cases, by mouth. Whole proteins such as skin milk powder, casein, or lactalbumin probably serve best for oral use when possible, but protein hydrolysates administered frequently in small quantities by stomach tube are absorbed even more readily by a seriously ill patient. The administration of plasma transfusions is certainly of value but cannot serve as a method of correcting large losses of protein. Blood transfusions are of great benefit; the hematocrit, red cell, and hemoglobin values should be kept at a fully normal level.

Large quantities of carbohydrates must be supplied both orally and intravenously during the course of the disease, for their protein-sparing action as well as for satisfaction of the increased energy demands of the heightened metabolism. Together with a high carbohydrate intake, an appropriate balanced dosage of the B complex vitamins thiamine, niacinamide, and riboflavin are administered, since the physiologic requirement for these vitamins increases with febrile disease and with an increase in dietary carbohydrate.

Much improvement has developed in recent years in the antibacterial therapy of septicemia. Treatment of the disease itself was restricted not very long ago to the use of immune sera, specific antitoxins, and dyes such as acriflavine, gentian violet, and Mercurochrome, none of which proved of great value. The introduction of sulfanilamide in treatment of streptococcic septicemia marked the first great advance in chemotherapy of bacterial blood stream infections, and the use of sulfathiazole for generalized staphylococcic infections afforded a reliable method of attack on this form of the disease. Further improvements in sulfonamide therapy have followed.

At present, sulfadiazine is the most generally useful and least toxic of these drugs in the large dosage required for treatment of septicemia, although sulfathiazole may be somewhat more effective against staphylococci. These drugs are given orally in an initial dose of 4.0 Gm. (gr. 60), followed by 1.0 to 1.5 Gm. (gr. 15 to 22½) every four hours day and night, to maintain an effective concentration of the free drug in the blood approximating 15 mg. per cent. If oral administration is impossible, either drug as indicated can be given intravenously in the form of its

sodium salt, of which an initial dose of 5.0 Gm. in at least 100 c.c. of normal salt solution is injected slowly by intravenous drip. For administration by hypodermoclysis, a 0.5 per cent solution of the sodium salt in normal salt solution is used. Subsequent doses of 2.5 Gm. each are given in a similar manner at intervals of eight to twelve hours as required to maintain the optimum therapeutic level of the drug in the blood. Oral dosage is substituted for parenteral administration as soon as possible. Such dosage is continued until clinical recovery has occurred and the temperature has been normal for several days, after which the dose is progressively reduced by half every ten to fourteen days and is continued for at least two to three weeks after recovery. Withdrawal of the drug at the time of disappearance of symptoms is likely to be followed by recrudescence of the infection from hidden foci not yet obliterated. Use of the sulfonamide drugs is subject to the disadvantage that serious toxic effects (p. 279) may develop following such large doses, usually within a week or ten days after commencement of therapy. The patient must be watched closely for the earliest evidence of sulfonamide toxicity; if manifestations appear, the drug is discontinued at once and appropriate measures are instituted. There is some evidence that administration of sulfadiazine, sulfathiazole, and sulfamerazine in equal parts is equally effective therapeutically and less likely to produce toxic effects. The total dose of the combined sulfonamides is the same as that of any one of the drugs alone.

Penicillin is at least as effective as the sulfonamide drugs and probably more so in the treatment of septicemia due to susceptible organisms such as the staphylococcus, hemolytic or anaerobic streptococci, the pneumococcus, and perhaps the meningococcus and the clostridia. In treatment of septicemia, an initial dose of 50,000 units of penicillin is given intravenously together with 50,000 units administered intramuscularly. A maintenance dose of at least 25,000 units is given intramuscularly every two hours or 50,000 units every three hours, night and day. The response usually is prompt and satisfactory, but administration of penicillin should be continued for at least four or five days following clinical recovery. After this time the drug can be given orally in tablet form or intramuscularly in oil and wax, if preferred, for another week or more. It is probably a good plan to administer

both penicillin and a sulfonamide simultaneously in full dosage in treatment of septicemia caused by an organism susceptible to these drugs.

Like the sulfonamides, penicillin is of little or no value in septicemia due to gram-negative organisms except to reduce the number of other organisms acting as secondary invaders. Streptomycin is the drug of choice in management of blood stream infections caused by gram-negative bacteria, and the clinical response to the drug usually is gratifyingly prompt. Because susceptible organisms may develop tolerance or resistance to streptomycin very rapidly, perhaps within a day or two, if insufficient doses are given, administration of full therapeutic amounts of the drug is advisable from the beginning of treatment. Streptomycin is too toxic to permit intravenous use; the dosage advised in serious infections amounts to 0.33 to 0.50 Gm. given intramuscularly every four hours for from five to ten days. Administration of streptomycin is continued for several days after full clinical recovery has occurred.

### Respiratory Tract Complications

Like most other postoperative complications, those involving the lungs are more easily prevented than cured. The simpler irritative manifestations in the upper respiratory tract and in the main bronchi following inhalation anesthesia are not uncommon and usually are of short duration, responding readily to ordinary care. On the other hand, a seemingly mild tracheobronchitis may be the starting point for a progressive consolidation of a large area of lung tissue and must be watched with suspicion.

Pulmonary complications are much more common and more serious in men than in women; perhaps the fact that respiration in the female is predominantly costal in type, while that in the male is chiefly diaphragmatic, may be a contributory factor. However, it is certain that men, particularly those who smoke, are more commonly affected by chronic respiratory infections such as bronchitis and bronchiectasis, which may be of etiologic importance. Before operation is undertaken, any history of previous lung disease should be investigated and a roentgenogram of the chest should be made whenever indicated. The presence of any clinically evident pathologic change in the

lungs or the presence of cardiac deficiency requires a particularly careful watch for the development of pulmonary complications during the postoperative period.

Coryllos,<sup>1</sup> after considerable study, has stated that the postoperative pulmonary complications usually described as bronchitis, atelectasis, and pneumonia generally follow one another in a progressive manner, without definite distinguishing characteristics, and "represent evolutionary phases of one and the same postoperative pathological process—bronchial obstruction." The primary initiating factor responsible for the development of such pulmonary lesions is the exudation of bronchial secretions occurring so commonly in patients following anesthesia. He further asserts, with profound justification, that, since these states may merge imperceptibly into one another, energetic treatment at the earliest stage is of the utmost importance.

Other investigators believe that pulmonary complications following operation are more likely to be due to aspiration of nasopharyngeal secretions containing pathogenic organisms which may then gain a foothold in the lung parenchyma because of the patient's temporarily decreased resistance. The third etiologic theory that has received some consideration is that emboli arising from thrombosed veins in the operative area are chiefly responsible for the development of postoperative lung manifestations, the severity of the pathologic process depending upon the number and size of the emboli and upon the presence of pathogenic bacteria. Probably each of the three mechanisms is a factor, the proportionate importance varying in different cases, but it must be recognized that the presence of improper aeration of the lungs and consequent atelectasis are often the starting points of a progressive and serious postoperative pulmonary consolidation.

#### PULMONARY ATELECTASIS OR MASSIVE COLLAPSE OF THE LUNG

Development of a sudden rise in temperature and pulse rate during the first two or three days after operation is often due to pulmonary atelectasis or massive collapse, probably the commonest serious postoperative lung complication. It is generally agreed that this condition follows the development of a mucous

occlusion of the main bronchus or of the smaller bronchi leading to the lobe of a lung, with complete obstruction of the air passage. The alveolar air behind the point of obstruction is soon absorbed, the rapidity of absorption depending on the extent of lung tissue involved. Consolidation and exudation proceed in the unexpanded and airless portion of lung, a pneumonitis resulting. A secondary causative factor in the development of consolidation is the presence of venous stasis, due to local impairment of the pulmonary blood circulation as a result of inadequate alveolar inflation. If the obstruction is not soon relieved, the bacteria normally present in the bronchi may initiate a peribronchial inflammation, with subsequent development of lobular pneumonia (Figs. 21 and 22)

**Diagnosis.**—The picture is a characteristic one and diagnosis is not usually difficult, although the condition is frequently overlooked because it is not kept in mind. Onset is rather rapid, with a sharp rise in temperature and in pulse and respiratory rates. Pain in the chest over the affected area is inconstant, but it may be present. The degrees of dyspnea and of cyanosis depend on the extent of pulmonary tissue involved and neither manifestation may be much in evidence. When only a small portion of a lobe is involved, neither the physical signs nor the clinical picture may be striking; the condition may remain unrecognized unless a lobular pneumonia develops later. If the major portion of a lobe is blocked off by a mucous obstruction in a main bronchus, however, a considerable degree of collapse may be present, in which case the patient becomes ill very rapidly.

Physical signs also depend upon the extent of lung involved. At first, over a small area of involvement, little can be noted locally on examination. If a large portion of lung is collapsed, however, decreased expansion of that side of the chest may be observed and the intercostal spaces may be seen to retract on deep inspiration. The mediastinal contents are shifted toward the involved side because of the alteration in pressure relations, the degree of shift depending upon the degree of pulmonary involvement. With a pulmonary collapse on the right side the apex impulse of the heart is seen to be displaced toward the midline; with a left-sided atelectasis the cardiac pulsation is seen more laterally than normal. Mediastinal shift and the elevation

**LOBULAR COLLAPSE**  
 (PATCHY ATELECTASIS)

**LOBAR COLLAPSE**  
 (ATELECTASIS ONE LOBE)

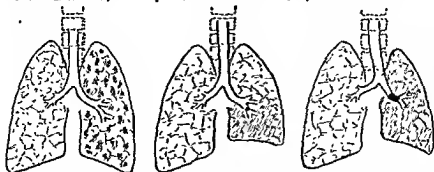
**MASSIVE COLLAPSE**  
 (ATELECTASIS ONE LUNG)


Fig 21.—Pulmonary atelectasis: varying portions of lung collapsed due to different positions of obstructing plug (From Eversole, U. H. S. Clin North America 24: 515, 1944, W. B. Saunders Co.)

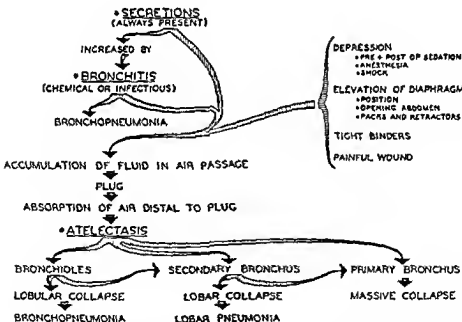


Fig 22.—Pulmonary atelectasis: probable course of events in development of bronchial or bronchiolar obstruction with subsequent atelectasis. (From Eversole, U. H. S. Clin North America 24: 515, 1944, W. B. Saunders Co.)

and fixation of the diaphragm on the side of the collapsed lung may be confirmed by percussion. If the atelectatic area is large or if it increases in size, dullness to percussion and diminution of breath sounds will be evident over the airless lung segment. Coarse bubbling râles and sticky wheezes may be audible over an entire side of the chest and perhaps over both sides. A per-



Fig. 23 — Postoperative atelectasis, right lung. Note displacement of mediastinum and elevation of right leaf of diaphragm.

sistent, ineffective, wet cough may be present. X-ray examination within several hours after onset of pulmonary atelectasis (Figs. 23 and 24) shows a diffuse mottling or, less commonly, a triangular shadow of the affected area, with the apex near the point of obstruction and the base toward the periphery of the lung, most often in the lower lobes. Both posteroanterior and lateral plates should be made if possible.

Later, as infection spreads outward from the bronchioles of the collapsed area, the sputum becomes purulent and is coughed up, and lobular pneumonia may develop. In such a case the patient becomes toxic and the characteristic physical signs of pneumonia appear.

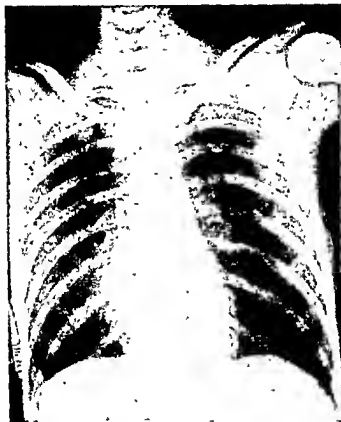


Fig. 24—Postoperative atelectasis following bronchoscopic aspiration of mucus from tracheobronchial tree (compare Fig. 23)

Frequently such a small area of lung is involved that little general effect is evident. In some cases the involvement may appear to be nothing more than a transient tracheobronchitis, accompanied by a moderate elevation of temperature and pulse rate for a day or two. The true nature of the process can be ascertained by thorough and frequent examinations of the chest, the physical signs being typical but occurring over a relatively small area.



Asthma and allergy may be contributory factors; patients afflicted with protein sensitivity are particularly subject to edema of the bronchial mucosa and spasm of the bronchial smooth muscle. Special precautions should be taken with these individuals.

**Prophylaxis.**—It has been demonstrated and confirmed many times that postoperative pulmonary complications are more likely to develop in patients who are in poor general condition before operation. Measures such as the administration of fluids intravenously, transfusion of blood, and use of specific medications to correct nutritional deficiencies and systemic weaknesses also will serve to decrease the likelihood of a pulmonary complication after operation.

A long-established axiom of surgery is that no elective operation should be performed on a patient suffering from an upper respiratory tract infection. Although no untoward result may occur, the possibility of spread of the infection with a resultant bronchopneumonia after operation cannot be ignored. Surgery should not be attempted until at least ten to fourteen days after the patient's complete recovery from the respiratory tract infection. Oral and dental infections, which may contribute to the development of postoperative atelectasis, bronchopneumonia, or lung abscess, should be corrected as far as possible before operation, especially if an upper abdominal incision is to be made.

Most adult patients, particularly those who smoke, normally clear a little mucus from the throat each morning upon arising. It is probably worth while for any patient who can do so to get out of bed on the morning of operation, walk at least a few steps, take several deep breaths, and cough up any tracheobronchial mucus that may have accumulated during the night.

Any factor that tends to depress the rate or amplitude of respiration after operation will encourage development of atelectasis. If preoperative sedation is used, only enough of the drug should be given to produce drowsiness; large doses may cause severe and prolonged depression of respiration and of reflexes. Aspiration of fluid during induction of inhalation anesthesia then may occur and the persistence of respiratory depression after recovery may hinder the expulsion of bronchial exudates. This is especially true of long-acting sedative drugs such as tribromethanol (Avertin).

Statistical studies show that the type of anesthesia has no constant relation to the development of lung complications; atelectasis and postoperative pneumonia follow operations performed under spinal anesthesia as often as those performed under all types of general anesthesia. This is true, however, only when general anesthesia is administered expertly and postoperative care is of the best type; work by Dripps and Deming<sup>2</sup> indicates that unless a rational and well-planned prophylactic regimen is followed, general anesthesia is more likely to be followed by respiratory tract morbidity than spinal or regional anesthesia.

Position of the patient during operation may have some relation to postoperative pulmonary atelectasis. In the Trendelenburg position, gravitational pressure of the abdominal viscera tends to elevate and immobilize the diaphragm, and in the lateral position, such as is used for intrathoracic or kidney operations, expansion of the lung on the side next to the table is hindered. During use of the lateral position, accumulation of bronchial exudate and of aspirated material may occur in the bronchial tree of the dependent and compressed lung. This is of particular significance during thoracotomy for surgical treatment of pulmonary suppurative processes such as bronchiectasis, lung abscess, or tuberculosis. In operations for these conditions, the head of the table is kept lowered to promote drainage downward toward the pharynx rather than into uninvolved lung; the anesthetist is prepared to bronchoscope the patient promptly if necessary during operation.

Type and location of the operative incision also are contributory factors. Upper abdominal incisions, especially those which require splitting of the rectus muscle high near the diaphragm, decrease the vital capacity of the patient much more than do lower abdominal wounds. Transverse incisions seem to cause less pain on respiration, an advantage stressed by those who favor this type of operative approach. The lateral overlapping of fascia for the repair of umbilical hernia has been largely superseded by the Mayo type of transverse fascial overlap because of the greater temporary reduction in vital capacity produced by the former procedure, with a correspondingly greater incidence of postoperative pulmonary complications. Insufficient aeration of the lungs is noted frequently also after operations on the stomach and biliary tract; postoperative pulmonary complications are

perhaps the commonest cause of death following major surgery of the upper abdomen.

Upper abdominal incisions have a relatively high incidence of postoperative herniation, both immediate and late; also, they are closed under relatively greater tension. For these reasons the entire upper abdomen and the lower chest wall sometimes are strapped tightly with broad strips of adhesive tape following operation. This procedure, while it may support the wound, also immobilizes the abdominal muscles and interferes with the descent of the diaphragm. Respiration then is chiefly costal in type and the lung bases, normally expanded through motion of the diaphragm, remain uninflated. Bronchial secretions collecting in these dependent portions therefore are expelled with difficulty. Adhesive strapping should be used simply to fix the dressings and should not immobilize the costal margins.

Cantheter aspiration of the secretions remaining in the patient's trachea, mouth, and nose should be performed routinely by the anesthetist at the conclusion of operation under general anesthesia. Bronchoscopic aspiration is indicated occasionally as a prophylactic measure, for example, following intrathoracic operations; large quantities of secretion frequently can be recovered from the bronchial tree in this manner in such cases. The prophylactic value of forced hyperventilation by administration of carbon dioxide immediately after operation has been clearly proved statistically by some to be of great value and by others equally clearly to be of no value whatever. Until more series are reported, no final satisfactory conclusion can be drawn except by those who have carried out the investigations themselves. Since the treatment certainly does no harm and may do good, it is a justifiable procedure following operations which may be complicated by atelectasis (if not used as a routine measure).

When used immediately after an operation, carbon dioxide can be given in 5 to 10 per cent concentration in oxygen, administered by the anesthetist until deep respirations begin, which usually occurs within two to three minutes. This procedure helps to aerate the basal portions of the lungs, clear the tracheo-bronchial tree of retained secretions, and hasten the elimination of a volatile anesthetic. It is probably useful also following spinal anesthesia in order to encourage expansion of the basal

portions of the lungs. As previously mentioned, administration of a similar gaseous mixture can be carried out when indicated at intervals of one to three hours after the patient has been returned to his room. Dripps and Deming<sup>2</sup> prefer the use of 100 per cent carbon dioxide administered every twenty to thirty minutes for the first six hours after operation by means of a catheter held several inches from the patient's nose. The gas is administered until the patient begins to breathe deeply, although he should not be made to pant violently. It is probably unnecessary to add that a surgical patient should not be awakened from a normal sleep to carry out a treatment of this type. When the necessary equipment is not available, a similar although less effective result may be attained by applying a paper bag over the patient's nose and mouth (p. 342) or by requesting him to take a dozen or more deep breaths at regular intervals.

The patient's position should be changed every hour or two while he is awake to encourage proper ventilation of the lungs. Many surgeons consider this procedure to be of more value in prevention of atelectasis than the use of carbon dioxide. All agree that it is a measure of great importance, especially in elderly, debilitated, or obese patients. One of the greatest advantages claimed for early ambulation is that the patient's reduced vital capacity is restored more quickly toward normal and that both the pulmonary circulation and pulmonary aeration are improved. A reduction in incidence of postoperative pulmonary complications consequently follows. Obviously, the presence of pulmonary infection or disease contraindicates early ambulation, however.

**Treatment.**—After establishment of the diagnosis of pulmonary atelectasis, therapeutic measures should be instituted immediately to prevent the subsequent development of lobular pneumonia, a highly dangerous complication, especially in aged or weakened individuals.

Frequent changes in position are mandatory. If the operation does not contraindicate it, the patient may be placed flat or upon the unaffected side, with his head a little lower than his feet to promote drainage. Several deep breaths in this position may loosen the bronchial secretions enough to permit them to be coughed up (Fig. 25). At times a thump on the back over the

diseased area will aid in loosening the obstructing exudate. Most effective of all the simpler procedures is the use of 5 to 10 per cent carbon dioxide in oxygen or of 100 per cent carbon dioxide administered as described, preferably with the patient lying on the unaffected side. The sudden expulsive effort of coughing causes such pain in the incisional area, however, that the patient may be reluctant to cough vigorously. Firm pressure with the palms of both hands over the incision by an attendant will help to support it against the sudden muscular strain of coughing. Constant inhalation of steam, medicated with compound tincture of benzoin, may help to loosen the mucus.



FIG. 25.—Postural method for relief of bronchial obstruction in postoperative pulmonary atelectasis. The patient lies in the Trendelenburg position, with the affected side uppermost, and coughs vigorously while the operative area is supported by a physician or nurse.

The use of oxygen alone, by tent, mask, or intranasal catheter, is not indicated, although at first sight it may appear to be of value. Certainly, the patient, somewhat cyanotic and breathing with difficulty, will be more comfortable in an atmosphere of 50 per cent oxygen, but the stimulus to deeper breathing and to coughing will be diminished. The obstructed areas of lung are then more likely to remain atelectatic and bronchopneumonia is more likely to develop. On the same basis, morphine or other sedatives which diminish the cough reflex must be used sparingly.

Sometimes the bronchial exudate is extensive enough to fill the entire bronchial tree on one or both sides. Respirations then are difficult, and coarse, sticky râles may be audible at some distance from the bed. If forced coughing, changes of position, and administration of carbon dioxide prove ineffective within one or two hours, aspiration of the obstructing mucus is necessary and should not be delayed any longer. This procedure is of the greatest value not only to treat pulmonary atelectasis in its early stages, but to prevent it from developing as a result of mucous occlusion of the bronchi.

The simplest, least troublesome, and most widely used method of tracheobronchial suction is the procedure described by Haight and Ransom.<sup>2</sup> No local anesthesia is used as a rule and the entire routine aspiration of the trachea and both stem bronchi requires only three or four minutes. A new rubber urethral catheter (Robinson, 16 French) connected to a suction machine supplying 15 pounds of suction, is used. A collecting bottle is necessary, since from 10 to 20 c.c. of mucus may be obtained. A glass Y tube is interposed, with one arm left open, suction being applied only while the free opening is closed with a finger tip.

The patient is propped up in mid-Fowler position and the neck is flexed slightly. The tongue is grasped with gauze by the operator and is drawn forward to raise the epiglottis; the catheter is then passed through the nose and down to the larynx, a cough usually resulting at this point. The catheter is drawn back a little and, while the patient inhales deeply, is passed quickly beyond the larynx into the trachea. Quick introduction is necessary at this point because expulsive coughing efforts occur as soon as the catheter slides into and beyond the larynx. If passage is unsuccessful, another attempt is made to slip the catheter past the larynx during the deep inspiration which follows coughing. The tongue is held forward continuously to prevent the patient from swallowing. Onset of coughing and a hoarse voice when the patient tries to speak indicate that the catheter is properly placed in the trachea rather than in the esophagus.

Suction is not applied until after the catheter has entered the trachea. When passage is successful, the patient is quickly placed in the horizontal supine position and suction is applied for several seconds, the catheter being moved back and forth for

1 to 2 cm. to aspirate the tracheal secretions. Coughing usually results; if not, the patient is asked to take several deep breaths and to cough in order to bring up some of the bronchial mucus within reach of the catheter. Suction is applied again for several seconds, the catheter being moved about during aspiration. When the trachea is dry, the patient's head is turned slightly to the left and the catheter is passed into the right bronchus. Intermittent aspiration is continued, the catheter being introduced gently into the bronchus as far as possible, until the outer end of the catheter is two to three inches from the external nares. When the right bronchus is dry, the catheter is withdrawn to its original position in the trachea, the patient's head is turned sharply to the right, and the chin is slightly elevated. An attempt is then made to pass the catheter into the left bronchus, aspiration of which is performed in the same way.

Drainage of the smaller bronchi during aspiration is improved if the patient is turned on his side, with the catheterized side uppermost. Suction is not continued for more than five seconds at a time, to avoid removing all the air from the tracheobronchial tree with resultant dyspnea and cyanosis, and the patient is asked to take several deep breaths between each application of suction. Since tracheobronchial suction is highly unpleasant to the patient, all the necessary manipulations should be carried out gently and firmly but quickly and without the least waste of time; the entire procedure should take no more than three to four minutes. The increased pulmonary ventilation and freedom of respiration which follow are ample compensation for the discomfort. The procedure is one which should be familiar to every surgical practitioner and intern, and no hesitancy should be shown in utilizing it when the indication arises. Because the apparatus is so simple and the procedure so harmless and easily performed, it can be repeated as often as necessary during the first day or two following operation.

Many patients may be unable to cooperate and in some instances it may be too difficult to catheterize the trachea or bronchi; the procedure is one which must be performed entirely by the sense of touch. After the patient has had a short rest and has recovered from the unsuccessful attempt, suction aspiration of the tracheobronchial tree may be tried again under local anesthesia according to the following method:

The patient is placed supine with a hard pillow or folded sheet beneath the shoulders and the neck is hyperextended. A ball or pledget of sterile absorbent cotton is grasped in a pair of long curved forceps, dipped into a solution of cocaine (10 to 20 per cent), and compressed gently to remove the excess solution. The patient's tongue is grasped with a gauze sponge and pulled forward. The pledget is introduced into the pyriform fossa on one side and held there gently for from thirty to sixty seconds, occasionally against some resistance from the patient. The same procedure is repeated with a fresh sponge in the opposite pyriform fossa, after which a third sponge is applied lightly to anesthetize the vocal cords. Gentleness is necessary in these procedures. Finally, 1.0 c.c. of cocaine solution (5 per cent) is dropped from a long syringe over the base of the tongue into the trachea. Occasionally these manipulations alone will induce sufficient coughing to bring up the offending mucus. The catheter is inserted into the trachea as previously described. If difficulty is encountered, the patient's head is hyperextended as much as possible, a moist gauze pad is placed over the lower teeth, a laryngoscope is introduced sufficiently far to lift the epiglottis, and the catheter is guided past the vocal cords by means of a long curved clamp<sup>4</sup> under direct vision (Fig. 26). All the secretions in the trachea down to the point of bifurcation can be removed in this manner. Aspiration of the main bronchi is attempted as outlined in the foregoing, although if the patient is uncooperative, it may prove too difficult.

Bronchoscopy will be necessary if the patient has an extensive atelectasis and the previously outlined procedures prove unsuccessful. The steps preliminary to bronchoscopy, including application of local anesthetic, are the same as those described. The bronchoscope is passed beyond the vocal cords under direct vision through a laryngoscope, after which the laryngoscope is withdrawn. A few drops of cocaine solution (5 per cent) are dropped into the lower trachea through the instrument and by gentle manipulation the opening of each lobe bronchus can be seen and the occluding secretions aspirated. If aspiration is done early in the course of the disease process, a surprisingly large quantity of exudate may be aspirated and the patient will recover almost at once, sometimes in a spectacular manner. If



aspiration is postponed too long, inflammation of the bronchial walls may develop, with subsequent bronchopneumonia.

Either penicillin or sulfadiazine is given in full therapeutic dosage as soon as the diagnosis of atelectasis is made, in order to prevent development of secondary bronchopneumonia.

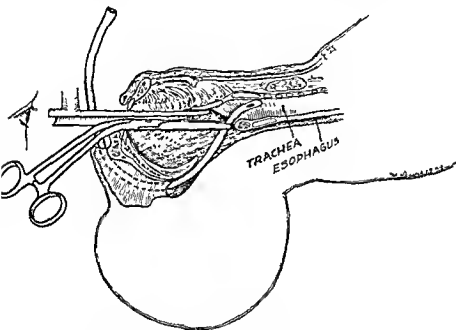


Fig 26 —Tracheobronchial suction — method of guiding aspirating catheter into the trachea under direct vision (From Eversole, U H S Clin North America 24: 515, 1944, W B. Saunders Co)

### BRONCHOPNEUMONIA

When lobular pneumonia develops, the help of a qualified internist is required. Progression of the pulmonary pathologic process from atelectasis to pneumonia may be recognized by the continued elevation and possibly the steady rise of temperature, pulse rate, and respiratory rate, with systemic evidences of definite toxicity.

After several days the patient usually will begin to cough up the bronchial exudate, the character of which changes from mucoid to purulent. As the breath sounds reappear over lung areas

formerly silent, they are noted to have a tubular quality, with a prolonged expiratory phase. Coarse and fine râles are present, with bubbling and sticky râles still evident over the larger bronchioles and bronchi. Leucocytosis becomes marked, the white cell count rising to 15,000 or more, with the increase chiefly in the neutrophilic leucocytes, young forms being somewhat increased.

When the pathologic process has progressed to this point, adequate supportive measures and careful nursing are needed. Sulfonamides and penicillin are of the greatest possible therapeutic value in cases of this type, and much reduction in mortality has been possible since these drugs have come into general use. Too much should not be expected of drug therapy in bronchopneumonia secondary to atelectasis, however; the pathologic process is not entirely an infectious one. The best treatment for this complication still is prevention; prophylactic measures should be taken routinely to prevent the development of postoperative atelectasis.

Penicillin is given intramuscularly in doses of 25,000 units every two hours or 50,000 units every three hours, day and night, and is continued for at least thirty-six hours after disappearance of signs and symptoms of the disease. Sulfadiazine probably is the most appropriate sulfonamide and is given orally in an initial dose of 4.0 Gm., followed by doses of 1.0 Gm. (gr. 15) every four hours. Sulfathiazole is the next best of the sulfonamides and is given similarly; sulfamerazine in the same dosage is also acceptable and is advocated by many clinicians. Combinations of the three drugs (p. 292) are acceptable. If the patient is too ill to take the drug by mouth, sodium sulfadiazine may be given slowly intravenously in an initial dose (for an adult) of 5.0 Gm. in 100 c.c. of sterile distilled water or normal salt solution, followed by half this quantity of the drug every eight hours until the patient is able to take it by mouth in the usual dosage, or the same quantities may be given by hypodermoclysis as a 0.5 per cent solution in normal salt solution. Toxic reactions to these drugs may occur and should be noted at their earliest appearance (p. 279). If pulmonary consolidation and bacterial toxemia progress to the point where there is danger to life, oxygen administration is instituted as a temporary measure.

Diet must be light, soft, easily digested, and attractively prepared; most of the foods permissible on liquid and soft diet lists may be used, except when contraindicated because of special operations. Efforts should be made to maintain the nutrition of the patient as well as possible. Patients unable to take food by mouth may be given dextrose solution (5 to 10 per cent) intravenously, preferably in small frequent doses of 500 c.c. rather than in large amounts at once. Fluid and salt balance must be maintained in the usual manner, using the optimum total daily urinary output of 1,000 to 1,500 c.c. as a guide. Slow administration intravenously each day of one or two liters of protein hydrolysate (5 per cent) solution containing dextrose (5 per cent) will be of value; this solution may be used as a substitute for simple intravenous dextrose solution. The lungs are examined carefully at frequent intervals to detect appearance of pulmonary edema; the appearance of widespread moist râles necessitates reduction in the use of intravenous fluids. Narcotics are used in minimal doses, if at all.

### ASPIRATION PNEUMONIA

With proper preparation of the surgical patient and improvement in anesthetic methods, pneumonia from aspiration of stomach contents has become uncommon. The complication carries a high mortality, pulmonary gangrene rapidly supervening as a result of the necrotizing action of gastric juice on the lung parenchyma.

*Aspiration of vomited material can be prevented almost entirely by placing the unconscious patient in proper position on return from the operating room. The Fowler position must not be used; if the head is elevated and the patient vomits as the effect of the anesthetic begins to wear off, aspiration will occur readily, aided by gravity. The subject should be placed horizontally, with his head turned to one side, and an attendant should be present to remove vomitus from his mouth as it is regurgitated.*

As in the case of any other pneumonic process, penicillin or an appropriate sulfonamide should be used. In a condition as severe as aspiration pneumonia, both penicillin and a sulfonamide should be given simultaneously in full dosage. There is little else

to offer with respect to drug therapy; if chemotherapy does not produce a satisfactory response, one or two intravenous injections of neoarsphenamine (0.3 Gm. in women, 0.45 Gm. in men) may be tried. The arsenical occasionally may help to control the growth of various spirillae and spirochetes, commonly found in pulmonary gangrene, but not much benefit can be expected from this drug.

The possibility of this complication must be considered in a patient who rapidly develops a serious pneumonitis early in the course of a stormy convalescence, in which persistent vomiting, dilatation of the stomach, hiccough, or intestinal obstruction plays a part.

### LUNG ABSCESS

Lung abscess is one of the less common pulmonary sequelae, but it may appear following any type of operative procedure. As a rule this lesion is more frequent after surgery upon the mouth or throat. Opinion is divided as to the mode of development; the most universally accepted opinion is that lung abscess develops following postanesthetic aspiration of infected material from the upper respiratory tract, with occlusion of a peripheral bronchiole. Bacterial gangrene develops rapidly and extends into the parenchyma of the lung through the necrotic bronchiolar wall. An alternative theory considers the lesion to be of embolic origin, a tiny infarction developing and forming a gangrenous area that ruptures into a bronchiole. Contamination with bacterial flora characteristic of the upper respiratory tract is thought to be secondary in such a case.

The lesion itself is a rapidly putrefying gangrene of the involved area, with a surrounding zone of marked pneumonitis. As the necrotic area liquefies, a cavity develops. Erosion of a bronchial wall soon occurs and the contents of the cavity are coughed up.

**Symptoms.**—Clinically, the onset of symptoms may be mild and the disease may be mistaken for an early bronchopneumonia or an acute upper respiratory tract infection. Several days after onset, a dry, persistent cough appears, accompanied by systemic evidences of an infectious process, such as loss of appetite, listlessness, slight fever, and chilliness. There is oc-

patients at or past middle age who were forced to remain in bed for relatively long periods. Only a few of these patients developed symptoms referable to thrombosis. Pulmonary embolism was responsible for 3 per cent of the deaths in the entire series, although nonfatal pulmonary emboli occurred in several times this number. Similar findings have been reported by other authors.

Until recently progressive venous thrombosis and thrombophlebitis were believed to develop in a large venous channel of the pelvis or upper thigh in which the slow current of venous blood, disturbed at the entrance of many tributary branches, developed eddy currents, followed by local deposition of platelets and fibrin, with subsequent formation of a secondary propagating thrombus. Present opinion is that venous thrombosis begins in the lower leg, most probably in the deep veins of the calf muscles, with progressive extension upward into the larger veins of the thigh and pelvis. Bauer,<sup>6</sup> after phlebographic studies in nearly 600 patients, concluded that thrombotic disease of the lower extremities begins in the veins of the calf muscles in 98 per cent of the cases.

The thrombotic process, once begun, extends proximally from the site of origin, the clot growing along the lumen of the vein in the direction of the blood flow (Fig. 27). As the mass builds up, the propagating portion becomes jellylike and soft, so that it may be difficult to distinguish where clot ceases and fluid begins. Early in the course of the process the clot is adherent to the vein wall only at the point of origin; the entire length of the femoral vein soon may be filled with a soft thrombus, attached precariously at its distal end and freely moving in the venous current. Growth and extension of the clot may proceed rapidly up the iliac vein to the inferior vena cava, the sole point of attachment in the early course of the process still being at the site of original development in the lower leg. Detachment of the head of the thrombus practically never occurs; emboli develop from the soft, almost semiliquid body and tail, which may break off at any time and be swept along the venous current to the right side of the heart and thence to the pulmonary artery. Thrombosis will not often develop in a strong current; in fact, a thrombus forming along a weak venous current may stop growing when it meets a rapid stream.\*

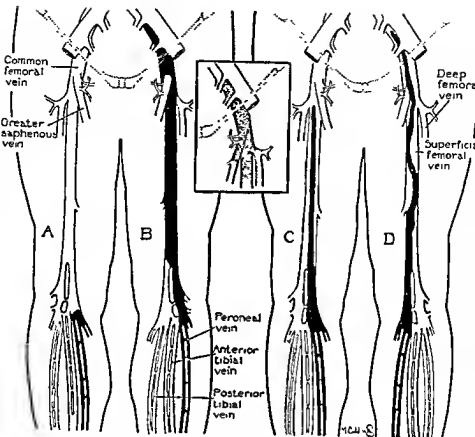


Fig 27 —Diagrammatic sketches showing various courses which a deep lower leg quiet thrombosis (phlebothrombosis) may follow. In each case the disease is shown as starting in one of the three main venous systems of the calf. A, The quiet thrombosis is represented as having failed to progress above the popliteal or femoral vein. B, The quiet thrombosis has progressed into the femoral vein where it now fully obstructs the femoral and external iliac veins and is represented as ending cleanly at the junction of the common iliac and hypogastric veins—a present-day conception of femorofemoral thrombosis or phlegmasia alba dolens. No attempt is made to indicate the inflammatory reaction about the great vessels or the involvement of collateral channels. (The insert represents an older conception of femorofemoral thrombophlebitis, starting in the region of the groin and spreading distally for an indefinite distance into the superficial femoral vein.) C, The thrombosis has formed a propagating floating mass not adherent to or obstructing the femoral vein. Its proximal end might or might not be seen on opening the superficial femoral vein at the groin. At this stage a fatal pulmonary embolism is seriously threatened. D, The thrombosis has reached a fairly advanced stage, being adherent to, without obstructing, the femoral vein and having extended through the left external iliac into the common iliac vein. At this stage emboli of fair size may readily be detached. (From Homans; Surg. Gynec. & Obst. 79: 70, 1914.)

Formation of the soft, growing thrombus is a rapid process, occupying only a few hours, or at most several days. Almost no symptoms may be noted during this time when the extending clot is free in the lumen of the vein but does not occlude it. At this stage the danger of pulmonary embolism is greatest and the clinical and subjective evidences of thrombosis are least. Any portion or all of the clot may be dislodged without cause or without warning and produce a pulmonary embolism, often the earliest indication that venous thrombosis has developed. Fortunately, however, the clot usually *remains attached*, grows until it fills the lumen of the vein, and becomes adherent to the intima. If the process is not too extensive, no interference with venous drainage may result and the patient may never know that he has had a venous thrombosis. In other cases, complete occlusion of the common femoral and iliac veins occurs, with the production of marked edema, swelling, and pain in the thigh and leg (phlegmasia alba dolens or milk leg). While the local symptoms are more severe in these patients, there is less likelihood of pulmonary embolism since the intravascular clot rapidly becomes adherent to the inflamed intima.

The different picture presented by quiet venous thrombosis (phlebothrombosis) on one hand and acute thrombophlebitis on the other has been explained in different ways. Homans<sup>7</sup> and Bauer<sup>8</sup> believe acute thrombophlebitis to be little more than a *secondary development from progressing venous thrombosis*, in which the vein becomes occluded completely by the clot, organization between the thrombus and the venous intima occurs, aseptic phlebitis and periphlebitis appear, and fever, tenderness, pain, and vasospastic reflexes result. The main difference between quiet thrombosis and acute thrombophlebitis (phlegmasia alba dolens) therefore lies in the presence of inflammatory reaction in the femoral and iliac veins in the latter condition. Other writers maintain that phlebothrombosis and thrombophlebitis are two separate and distinct pathologic entities. Ochsner<sup>9</sup> states that the mechanism of clotting in the two conditions is on an entirely different basis, inflammatory changes in the vascular endothelium acting as the direct cause of clotting in thrombophlebitis and *two other factors* (increased coagulability of the blood and slowing of the blood flow) being responsible for intravenous clotting in phlebothrombosis. The

latter author further states that intimal attachment and organization of the loose intravascular clot in phlebothrombosis occurs infrequently in the early stages of the disease, as maintained by Bauer, and that this should not be depended upon to diminish the likelihood of pulmonary embolism.

Complete occlusion of the common femoral or external iliac vein with phlegmasia alba dolens may produce chronic edema of the affected extremity. In some cases the femoral vein recanalizes, but since the valves are destroyed by the organized clot it is doubtful whether the reopened vein improves venous drainage or increases venous reflux<sup>9</sup> because of valvular insufficiency. Most of the return blood flow in these patients is diverted through normally small collateral channels which enlarge sometimes to great size.

Although the primary etiology of postoperative intravenous clotting has not been finally explained, three factors contributory to its development<sup>10</sup> have been recognized; namely, retardation of the venous flow, increased coagulability of the blood, and inflammatory changes in the walls of the veins. The most important of these is undoubtedly venous stasis in the lower extremities as a result of muscular inactivity, postoperative circulatory and respiratory depression, and perhaps increased intra-abdominal pressure from tight dressings or from intestinal distention. Hunter and associates<sup>3</sup> have stated that "the greatest single factor favoring thrombus formation in the lower extremity is sudden confinement to bed of a previously ambulatory older person without the benefit of exercise or the aid of gravity in the maintenance of an efficient venous circulation." The depressing effect of increased intra-abdominal pressure upon venous return from the legs is especially marked when the patient is kept in Fowler's position, which accentuates venous stasis in the pelvis. It is possible also that the common femoral and popliteal veins may be compressed as a result of the concomitant flexion of the thighs and legs, particularly if a pillow is placed below the knees. Shallow respirations because of pain in the operative incision also tend to decrease the rate of venous flow to the pulmonary circulation and consequently to retard the rate of flow in the veins of the lower extremities.

However, slowing of the venous return is not enough in itself to cause intravascular clotting. There is an increase in coagula-



bility of the blood following injury, surgical operation, or parturition which acts as a contributory factor in the development of venous thrombosis. The explanation for the increased clotting tendency is not clear; it may be due to a combination of causes such as operative trauma with release of thromboplastin and increased agglutinability of the blood platelets, dehydration with hemoconcentration and increased blood viscosity, and changes in the plasma proteins, with elevation of the fibrinogen and globulin. A rise in platelet count occurs following trauma of any type but cannot in itself be responsible for postoperative intravascular clotting. Venous thrombosis may occur at any time between the first day and the fourth week after operation, while the postoperative rise in blood platelets appears after the fourth day as a rule, reaches its height by the tenth day, and disappears within two to three weeks. It is probable that the increase in platelets contributes to the growth and propagation of the clot, however, once it has begun to develop.

Other changes in blood components immediately following operation also have been noted; for example, an increase in plasma prothrombin and an increase in heparin tolerance. DeTakats<sup>11</sup> has proposed the use of a heparin tolerance test to identify patients who are likely to develop postoperative venous thrombosis and has reported some success with its use. Briefly, the test consists in the administration of 10 mg. of heparin (1.0 c.c.) intravenously and the determination of coagulation time by the capillary tube method before the injection and ten, twenty, thirty, and forty minutes after. The results are plotted as a graph. If the coagulation time does not rise above  $4\frac{1}{2}$  minutes and the curve is flat following injection of heparin, the response is considered subnormal, indicating an increased tolerance to heparin and a possible tendency to venous thrombosis. If the coagulation time following injection of heparin reaches or exceeds  $7\frac{1}{2}$  minutes, the patient is classed as a hyperreactor, showing sensitivity to heparin, with less likelihood of developing phlebothrombosis. Patients of this group are likely to show clinical evidences of heparin sensitivity such as flushing, dyspnea, or faintness and may require relatively small doses of the drug if its use should become necessary later. Various other laboratory tests have been proposed for the identification of patients in whom postoperative thrombosis is likely to occur, but none has

been devised that is sufficiently simple and yet accurate enough to be dependable.

Damage to the endothelium of the veins will be followed by intravascular clotting in most cases, although other contributory factors such as retardation of blood flow also are necessary to establish clinical thromboembolic disease. Although most investigators believe that simple thrombosis may progress and develop into thrombophlebitis, with intimal irritation and inflammation resulting from organization of the clot, others<sup>8</sup> maintain that the two conditions are separate entities and that intimal injury by bacterial invasion, by toxins, or by allergic sensitization precedes the development of thrombophlebitis. Whatever the true explanation may be, it is certain that in the inflammatory form the intravenous clot is more firmly fixed and less likely to produce an embolus, although the possibility is still present.

Other contributory factors include older age, obesity, cardiovascular disease, debility, malnutrition, anemia, foci of infection, varicose veins, inflammatory lesions of the lower extremities, and possibly the vague quality known as constitutional predisposition. Climate and season seem to play a part; the incidence of thrombosis and embolism has always appeared to be higher in the northern and New England states<sup>12</sup> than in the southern states, particularly in the spring and winter months. Vasoconstrictor drugs or agents such as tobacco may decrease the circulation in the extremities and therefore predispose to thrombosis. These factors are so common and so widespread that several at least will be found in almost all surgical patients. The use of well-planned and actively applied prophylactic measures is highly advisable therefore as a routine measure to prevent postoperative thrombosis.

**Diagnosis.**—Symptoms vary according to the type, extent, and stage of the process. Quiet thrombosis (phlebothrombosis) may produce no local symptoms whatever, the first evidence of the condition appearing as a pulmonary embolism. In most cases some suggestive evidence can be found on physical examination, such as slight tenderness to pressure over the muscles of the calf or over the medial aspect of the foot, often the earliest sign. Strong passive dorsiflexion of the foot may cause pain in the calf if thrombosis has developed in the muscle veins

(Homans' sign<sup>7</sup>). The region of the femoral vein in the upper thigh or inguinal area may be slightly tender to pressure. Dusky-ness or cyanosis of the foot may appear, with slight edema of the foot or ankle, perhaps evident only when the foot is in a dependent position. A slight unexplainable rise in temperature or in pulse rate is frequently the only indication of early thrombosis. Other patients, lacking even this evidence, may experience a transient attack of faintness or a slight fleeting pain in the chest. Such symptoms are strongly suggestive of pulmonary embolism; if they appear at any time in a patient confined to bed or just allowed to be up, immediate examination of the legs is indicated. Physical examination of the chest may not reveal signs of a minor embolism; a roentgenogram should be taken.

Subclinical venous thrombosis occurs frequently; if symptoms appear, however, the process has extended dangerously and demands immediate therapeutic measures. Most surgeons, particularly those who have had personal experience with the complications resulting from venous thrombosis, make a daily search for the earliest evidence of the process by questioning the patient concerning pain in the legs or chest, by examining the legs and feet, and by inspecting the chart for minor elevations of temperature or pulse rate. The diagnosis is not easy, however; fully developed and extensive venous thrombosis may be present in one or both lower extremities with no discernible signs of its presence.

Acute thrombophlebitis, in contrast, usually appears during or after the second postoperative week, the first evidence often being a febrile reaction (100 to 102° F.), frequently with a chill and a rise in pulse rate. When the inflammatory process is fully developed, spontaneous pain is present over the involved vein and may become severe, and a well-marked line of tenderness can be followed along the course of the vein from the middle of the calf along the inner surface of the thigh to the inguinal ligament. Thrombophlebitis of the saphenous vein alone is not accompanied by edema; thrombophlebitis of the common femoral or iliac vein is characterized by marked edema, which is sometimes the first localizing sign noted. In such a case the limb may become greatly swollen and so heavy that the patient is unable to raise it without assistance. Common femoral or iliac vein thrombophlebitis is a highly regrettable occurrence

since the affected leg may remain permanently swollen and functionally impaired. It is probable that in these cases the lymphatics in the inguinal region also are obstructed.

Much dependence was placed formerly on phlebography in the diagnosis of quiet venous thrombosis, a radiopaque substance being injected into the saphenous vein over the medial malleolus on the suspected side and roentgenograms of the calf and thigh taken immediately. Further study has shown that phlebographic examinations are often equivocal and misleading and their use has been largely abandoned in this country.

Prophylactic measures are simple and involve so little trouble that they should be instituted for every patient, particularly following operations in which the abdominal wall is incised or in which Fowler's position is used during convalescence. The procedures employed are directed chiefly toward the improvement of the circulatory return from the pelvis and lower extremities. Barnes<sup>11</sup> has detailed the routine postoperative program in use in one surgical service at the Mayo Clinic as follows:

"The patient is placed in the Trendelenburg position for the first twenty-four hours after operation. Carbon dioxide is administered by inhalation several times in the day and night for the first forty-eight hours. Frequent deep breathing exercises are urged in every case. Extreme care is observed to keep the patient's legs warm at the operation, during his transfer to his room, and after his return to bed. Frequent massage of the legs is practiced during the first forty-eight hours and twice daily thereafter until the patient is out of bed. Passive and active movements of the extremities are insisted on at stated intervals from the time the patient is returned to his room and until he is out of bed."

Gamble<sup>12</sup> has devised an exercising apparatus consisting of a pair of bicycle pedals attached to a board which he requires his patients to use daily, beginning on the second postoperative day. All are agreed that regular exercising movements of the legs are of the greatest value as a prophylactic measure and should be instituted in some form as soon as possible after operation.

Other routine measures are advocated to improve the circulatory return. Tight dressings on the abdomen should be avoided; Fowler's position should not be maintained uninter-

ruptedly for long periods; intestinal distention should be prevented by supplying the patient with solid food within the first few days after operation if possible or by introducing a duodenal tube if nausea and vomiting persist or distention develops. Proper ventilation of the lungs should be secured either by the administration of carbon dioxide at regular intervals or by the institution of deep-breathing exercises every hour or two, especially if the patient is receiving sedatives. Dehydration, which tends to increase the viscosity of the blood and to depress the rate of flow, must be prevented by maintenance of a proper fluid intake. All these measures, if followed carefully, tend to improve the general condition and strength of the patient as well as to forestall the development of venous thrombosis or thrombophlebitis.

Smoking, which induces vasoconstriction in the extremities, is forbidden for a week or more after operation and perhaps also for a few days before. Ochsner<sup>3</sup> advises the use of compression bandages (Ace bandage No. 8) in patients over 40 years of age, to be applied to both lower extremities from toes to groin before the patient leaves the operating room. It is stated that such supportive bandages, by compressing the superficial veins, increase blood flow through the deep veins and decrease venous stasis. Others<sup>22</sup> have advised the routine use of elastic bandages particularly in patients with varicose veins, the bandages to remain in place until after the patient is ambulatory.

Advocates of early postoperative ambulation claim that it produces improvement in circulation of the blood both in the lungs and in the lower extremities. Aged patients in particular do not tolerate confinement to bed; every effort should be made to get them up and about as soon as possible. For those who must remain in bed, frequent routine exercises of all four extremities and deep-breathing exercises are necessary. It is probable that many cases designated as "hypostatic pneumonia" begin as postembolic infarcts which might be prevented by routine prophylaxis as described. Despite the theoretic advantages, however, there have been few reports published in which early ambulation has lowered demonstrably the incidence of postoperative thromboembolic disease. To avoid any possibility of venous constriction, it is advisable to see that patients who arise and walk during the early postoperative period return to bed as soon as they

have stood up for a moment and taken a few steps; compression of the popliteal veins may occur if they are permitted to sit up in a chair.

More effective prophylactic measures may be necessary in individuals who have had previous attacks of venous thrombosis, in those who have a better-than-average expectancy of developing intravascular clotting, or in those who have sustained injuries or undergone operations which are likely to be followed by thrombosis. Methods of prophylaxis in current use include the administration of anticoagulants (heparin or dicumarol) alone,<sup>19 20,21</sup> ligation of the superficial femoral veins<sup>15</sup> bilaterally, or both.

DeTakats and Fowler<sup>10</sup> report the use of Prostigmin routinely after all laparotomies, particularly pelvic operations. It is stated that this drug, given hypodermically in doses of 1.0 c.c. (1:2,000 solution) every four hours for ten doses, not only decreases the tendency to postoperative intestinal distention<sup>1</sup> and bladder atony but also reduces an abnormally increased tendency to intravascular clotting.

**Treatment of Phlebothrombosis.**—Probably no field of surgical interest is subject to such divergent and actively controversial views as the management of thromboembolic disease. The discussion is complicated somewhat by the fact that clinical reports detailing the use of anticoagulant drugs and similar reports describing the use of operative procedures both claim equally good results. As is the case with many discussions of this type it probably is true that while either method will serve satisfactorily in most cases, there are a few situations in which one method is preferable to the other. There is a possibility also that when the causes and pathologic physiology of venous thrombosis are elucidated more completely, a simple method of prophylaxis or even of positive identification of susceptible individuals will be devised that will alter indications and use of both of the current methods of treatment.

*Heparin* may be used both for prophylaxis against venous thrombosis when there is a strong likelihood of its development and for treatment of thromboembolic disease already established. The original method of administering the drug by continuous intravenous drip, as suggested by Murray and Best,<sup>16</sup> is effective,

although disadvantageous. According to this method, a solution of the sodium salt of heparin is added to the infusion, from 100 to 200 mg. (10,000 to 20,000 units) for each liter of normal salt or dextrose solution. The resulting solution is allowed to flow into the vein at a rate, usually 20 to 25 drops per minute, sufficient to raise the clotting time of the patient's blood to fifteen or twenty minutes and maintain it constantly at that level. Coagulation time should be determined every four to six hours to make sure that the dosage of heparin is neither too large nor too small. Administration of heparin is not begun until at least six hours after operation to avoid interference with hemostasis in the operative field. The occurrence of internal or external bleeding must be anticipated during the first day or two and the infusion stopped at once should any evidence of hemorrhage appear. Administration of heparin by infusion must be continued without interruption for a minimum of ten to fourteen days or longer, until all indications for its use are past. It is worth noting that venous thrombosis may develop promptly in some cases as soon as heparin is withdrawn and that vigorous prophylactic measures and frequent careful examinations are necessary from the time the drug is stopped.

Heparin may be given in divided doses if preferred, 50 mg. (5,000 units) being slowly injected intravenously every four hours during the day and night for as long as necessary. While theoretically the heparin effect disappears within two hours after injection of each dose, the multiple injection method appears to be as effective clinically as administration by continuous intravenous drip. The patient is kept in bed for the first few days of anticoagulant therapy but is ambulatory thereafter. It is important to continue treatment without interruption for at least a week after the patient begins to walk about; if embolic episodes have occurred, anticoagulant therapy is continued in decreasing dosage for several weeks. Bauer<sup>6</sup> strongly advocates the use of heparin in treatment of thrombosis, preferring the method of intermittent intravenous injection. Murray,<sup>17</sup> Allen,<sup>22</sup> and Loewe and Hirsch<sup>19</sup> have reported strikingly successful results with the use of anticoagulant therapy alone, employing heparin with or without dicumarol, in the treatment of established venous thrombosis and of pulmonary embolism.

A method of administering heparin in a medium that permits slow absorption and release and therefore prolonged effect has been devised by Loewe and associates.<sup>13,19</sup> Pitkin's menstruum is used as the vehicle, the ingredients consisting of gelatin, dextrose, glacial acetic acid, and distilled water in proportions varying according to the amount of heparin added. The formula is made up to contain 100 mg. of heparin sodium per cubic centimeter, with or without added vasoconstrictors (epinephrine, ephedrine) to delay absorption. The preparations containing vasoconstrictors are usually employed, except in patients with cardiovascular disease or hypertension. The earliest preparations produced pain at the site of injection; this effect has been reduced by buffering to attain a more physiologically acceptable pH. The medication is supplied in ampules; dosage is regulated according to body weight and desired heparin effect. For administration, the ampule is placed in warm water (not hot) until the contents are fluid, and the ampule then is shaken. The dose is withdrawn into a warm sterile syringe and is injected deeply into the subcutaneous tissues of the thigh. Initial dose for patients weighing less than 150 pounds (67.8 kilograms) is 300 mg. of heparin sodium and 400 mg. for patients over this weight. This single dose accomplishes heparinization for two days as a rule; heparin effect may be continued as long as desired by repeating the dose every second day or in some cases every third day. Blood-clotting time is determined at least once a day by the Lee-White technique rather than by the capillary tube method. The authors point out that if a blood transfusion is given during heparin therapy, a dose of 300 mg. of heparin should be given immediately after transfusion, no matter what the previous dosage of heparin might have been. Continuous heparinization is continued for ten to fourteen days in simple thrombosis but is necessary for three or four weeks when even minor attacks of pulmonary embolism have occurred. It is necessary that the patient be out of bed and walking before heparin administration is discontinued, in order to prevent development of a clot immediately after withdrawal of the drug. Papaverine is supplied in doses of 0.06 to 0.09 Gm. (gr. 1 to 1½) every four hours intravenously or intramuscularly during the first day or two, after which similar maintenance doses are given by mouth. Smoking is forbidden, a precaution which is common to all plans



of treatment for thromboembolic disease. The authors remark that while the original thrombus is not decreased in size immediately by heparinization, progress is stopped, inflammatory changes subside, and the clot finally either resolves or organizes.

*Dicumarol*, an anticoagulant discovered in spoiled sweet clover and later isolated and synthesized, exerts its effect by decreasing the prothrombin concentration in the blood to the point at which hypoprothrombinemia occurs. Action of the drug develops slowly but is prolonged; after a single effective dose, no change occurs for one or two full days, following which the blood prothrombin progressively decreases. The effect reaches a maximum in from three to five days and then gradually diminishes, disappearing by the seventh to tenth day. *Dicumarol*, although a useful drug when employed with caution, is dangerous because of its cumulative effect. It should never be used unless blood prothrombin determinations by the Quick method (p. 221) can be performed at least once daily and unless transfusions of fresh whole blood and proper doses of synthetic vitamin K can be given at once if hemorrhage occurs or if the blood prothrombin level drops below a minimum of 10 per cent of normal. There are certain well-established contraindications to use of *dicumarol* under any circumstances. These include hepatic or renal disease, jaundice, hypoprothrombinemia present before the use of *dicumarol*, hemorrhagic tendency, open or granulating wounds, recent thoracic or neurosurgical operations, hypertension, hyperthyroidism, the presence of drainage tubes in the gastrointestinal tract, or the presence of medical disease requiring the use of salicylates, which also tend to produce hypoprothrombinemia. It is not used following prostatic surgery or during the puerperium. *Dicumarol* also may not be used if a surgical procedure is planned in the near future.

Within these limits, *dicumarol* is a useful drug in prophylaxis and treatment of venous thrombosis; its chief advantages over heparin include inexpensiveness, effectiveness by mouth, and prolonged action. The latter characteristic, of course, is occasionally a disadvantage. The effect of *dicumarol* varies with the rate of its absorption from the gastrointestinal tract; in some cases there appears also to be some individual sensitivity.

Dosage is controlled by determination of prothrombin time (Quick method) at least once daily; the dosage must be indi-

vidualized, since some patients require less of the drug than others. Dicumarol is given orally in an initial dose of 300 mg., followed by a dose of from 100 to 200 mg. on each succeeding day according to the level of prothrombin in the blood. Barker and his group<sup>10</sup> prefer to keep the blood prothrombin between 10 and 30 per cent of normal, administering or withholding a maintenance dose of 200 mg. of dicumarol according to whether the prothrombin level is above or below 20 per cent that day. Others prefer smaller doses; Evans and Boller<sup>21</sup> advise an initial dose of 200 mg. of dicumarol if the patient weighs less than 150 pounds (67.8 kilograms) or 300 mg. if the patient is heavier, to be followed in any case by a daily maintenance dose of 100 mg. whenever the blood prothrombin exceeds 65 per cent of normal. DeTakats and Fowler<sup>19</sup> advocate an initial dose of 300 mg. of dicumarol the first day, 200 mg. the next day, and subsequent dosage in sufficient quantity to maintain the blood prothrombin within a range of 60 to 30 per cent of normal.

For routine prophylaxis, dicumarol alone is sufficient; administration is begun on the fourth postoperative day. When used for treatment of thromboembolic disease, however, heparin also must be given during the first two days of dicumarol therapy, since the effect of the latter drug develops so slowly. Heparin may be given by the intermittent method, 50 mg. of the drug being injected intravenously every four hours, or it may be given as a single dose by the method of Loewe. According to the plan utilizing a single injection of heparin<sup>21</sup> in Pitkin's menstruum, a dose of 200 to 300 mg. of heparin is given in accordance with the patient's weight, and the first dose of dicumarol is given at the same time. The blood coagulation time is checked at intervals during the next two days and another injection of heparin is given if the clotting time approaches normal before dicumarol effect appears. Administration of heparin by intermittent doses rather than by a single slowly absorbed dose also requires regulation by frequent determinations of the clotting time until hypoprothrombinemia due to dicumarol develops. As soon as the effect of dicumarol becomes apparent, heparin is discontinued. When dicumarol is given alone, only the prothrombin time need be checked; when heparin is used also, both the prothrombin time and the coagulation time should be observed each morning.

The chief complication of anticoagulant therapy is hemorrhage, which may be either internal or external. Bleeding due to overdosage of heparin can be controlled by transfusion of fresh whole blood and administration of protamine<sup>27,29</sup> (p. 225) intravenously in a dose of 50 mg. for each 50 mg. of heparin to be neutralized. Hemorrhage complicating dicumarol therapy can be controlled by intravenous injection<sup>26</sup> of a large dose (64 mg.) of a soluble menadione derivative and by transfusion of fresh whole blood. Bank blood is not satisfactory, since the prothrombin content of stored blood decreases progressively during storage.

*Operative treatment of venous thrombosis* is advocated by many authorities on the basis that anticoagulant therapy can neither decrease the size of the thrombus already present nor decrease the likelihood of its detachment, with consequent pulmonary embolism. The validity of these arguments is not admitted, however, by the advocates<sup>18</sup> of anticoagulant therapy.

Interest in surgical therapy for quiet venous thrombosis has developed rapidly. Because phlebothrombosis almost always begins in the veins of the lower extremities, ligation of the superficial femoral vein<sup>7,10</sup> on the affected side is logically the procedure of choice. Further experience has revealed that in some cases fatal emboli may arise from the apparently unaffected extremity, even after ligation of the femoral vein on the side in which disease is apparent. Occasionally, also, repeated embolic attacks may appear in patients who present little or no evidence of venous thrombosis. For these reasons, many surgeons<sup>8,22,15</sup> advocate immediate ligation of both superficial femoral veins with removal of any clot that may be present if there is the slightest reason to suspect the presence of venous thrombosis in either leg.

Venous drainage of the leg is not impaired by ligation of the superficial femoral vein below the level of the deep femoral (profunda femoris) vein, since the collateral pathways between the deep femoral vein, the saphenous veins, and the smaller tributaries of the femoral vein are entirely sufficient. To be of maximum protective value, superficial femoral vein ligation should be performed as an emergency procedure as soon as possible after phlebothrombosis has been diagnosed or justifiably suspected.

In a small percentage of cases, clots arising in the deep femoral vein may produce pulmonary embolism even after the

superficial femoral veins have been ligated (Fig. 28) Various writers have advocated ligation of the common femoral vein<sup>12</sup> for this reason, even though persistent edema of the leg and thigh is likely to develop after operation. It is questionable, however, whether the added protection afforded by the higher ligation is worth the probability of permanent impairment of venous drainage in addition to the increased operative difficulty. In a few instances the intravascular clot is found to extend well up into

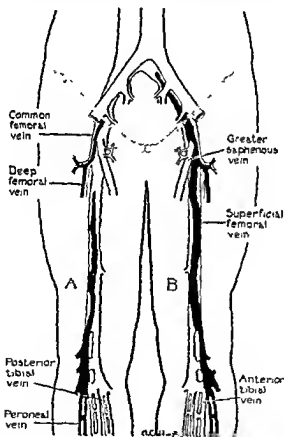


Fig 28 — Ologrammatic sketches of advanced stages of a quiet lower leg thrombosis. A, A propagating thrombus has advanced into the upper right femoral vein and at the same time an independent thrombus has started in the deep femoral vein (profunda femoris), propagating into the common femoral vein. Section of the superficial femoral vein would neither reveal nor control this second process. B, A propagating thrombus has become adherent to, without obstructing, the left femoral vein and has advanced into the common iliac vein. Its proximal end may easily be detached. An associated thrombosis is present in the deep femoral system. (From Romans Surg., Gynec & Obst, 79: 70, 1944)

the iliac vein and even into the inferior vena cava. Since such a thrombus may be difficult to extract through an opening in the femoral vein, the suggestion has been made by several writers that ligation of the common iliac veins on one or both sides or ligation of the lower portion of the inferior vena cava<sup>7 23 24</sup> may be preferable to the possibility of pulmonary embolism.

The development of surgical therapy for thromboembolic disease thus has passed through a series of stages in which operations of increasing magnitude have been proposed for control of the potentially dangerous clot. There can be little objection to the use of unilateral or even of bilateral superficial femoral vein ligation in treatment of quiet venous thrombosis; the operation is not difficult, subsequent venous drainage is not impaired, and, if the operation is done immediately when the diagnosis is made or suspected, it should afford a highly satisfactory degree of protection. Ligation of veins above this level is more permanently damaging to the leg, more difficult to perform, and more injurious to an already ill patient. Moreover, it is by no means certain that venous ligation at these higher levels offers enough added protection to compensate for its disadvantages. There is one pathologic state, however, in which ligation of the lower inferior vena cava offers the only hope of cure if antibiotics and chemotherapy fail. Suppurative thrombophlebitis in the pelvic or ovarian veins (for example, following septic abortion) will not always respond to chemotherapeutic drugs because of the presence of infected clots which act as inaccessible reservoirs of infection and produce showers of septic emboli. Collins and associates<sup>25</sup> have reported twenty-one cases of suppurative pelvic thrombophlebitis treated by ligation of the inferior vena cava and the ovarian veins, with only four deaths, two of which occurred after a lapse of several months. In these patients penicillin and chemotherapy had proved ineffective and operation was performed as soon as the progressive course of the disease became evident. No interference with circulation resulted and, surprisingly, no interference with function of the pelvic organs. Collins suggests the interruption of the sympathetic chain on each side during the course of the operation, which is performed by the intraperitoneal route, or, as a substitute, the postoperative use of lumbar sympathetic block.

Because of the somewhat incomplete protection against embolism afforded by ligation of the superficial femoral veins, even the surgeons who prefer surgical treatment<sup>12,15</sup> of phlebothrombosis advocate the use of heparin and dicumarol in small doses following venous ligation, as prophylaxis against subsequent clot formation above the ligatures. The final solution to the problem obviously has not yet been attained nor does it appear to lie in the direction of more extensive and serious operative procedures. At the present time, the best methods of treating phlebothrombosis appear to be either the use of simple anticoagulant therapy properly managed or the emergency ligation of both superficial femoral veins together with anticoagulant therapy following ligation. Nonoperative treatment is probably preferable if the clot has extended above the level of the common femoral vein and ligation at or above this point would be required; bilateral superficial femoral vein ligation is perhaps preferable if the thrombotic process is still in a relatively early stage or if the patient will be confined to bed for a long period. Routine postoperative prophylaxis by vein ligation or by use of anticoagulants in selected groups of patients is being advocated at present but has not yet been generally adopted. It is worth emphasizing that in no case should vein ligation ever be performed in treatment of acute thrombophlebitis; this type of thrombosis is managed only by nonoperative methods.\*

The technique of superficial femoral vein ligation (Fig. 29) is simple, but the operation should be performed gently to avoid dislodging the clot. The operating table is tilted slightly to incline the patient's feet downward in order to increase the filling of the femoral veins. Either local anesthesia (procaine, 1 per cent) or sodium pentothal can be used. A longitudinal or a transverse incision at least four inches long is made below the region of the saphenofemoral junction, the femoral artery is gently drawn laterally, and the femoral vein is exposed. Allen and associates<sup>26</sup> strongly recommend the use of a longitudinal incision, beginning at the inguinal fold over the site of the arterial pulsation and continuing downward over the course of the vessels for 8 centimeters. The longitudinal incision avoids damage to the inguinal lymphatics and permits rapid exposure of the vessels if accidental injury should occur, with profuse bleeding. According to the technique of operation advocated by

these authors, the superficial femoral vein is cleared gently from the surrounding tissues for an inch below the point of entrance of the deep femoral (profunda femoris) vein and two ligatures are passed around it but not tied, a slight bulbous dilata-

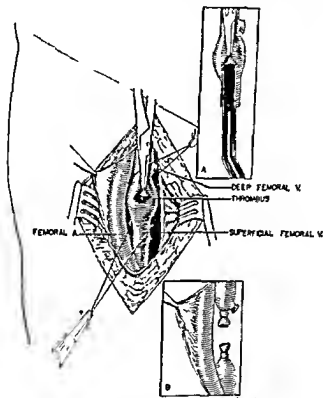


Fig 29 — Venous thrombosis: exposure of superficial femoral vein with thrombectomy. A vertical incision is used. The junction of the superficial and deep femoral veins is identified by a dilatation of the superficial vein just distal to the junction. The femoral artery overlies the vein in this area and is drawn laterally without being dissected completely free. Inset A shows aspiration of the thrombus with a glass cannula. Inset B shows the completely divided superficial femoral vein, each end doubly ligated with a ligature and a transfixion suture of cotton or silk. (From Allen, Linton, and Donaldson. *J A M A* 132: 1268, 1917.)

tion of the superficial femoral vein is normally visible just below the entrance of the profunda vein. Traction is exerted on the ligature loops in opposite directions to isolate the cleared segment of vein. The vein is incised transversely and any clot

visible in the proximal portion is aspirated by means of a glass suction tube (a sterilized drinking tube will suffice). After the clot has been removed from the upper end of the incised vein and free bleeding occurs, the upper ligature is tied, as close as possible to the junction of the superficial and deep femoral veins. The clot is removed similarly from the lower end of the vein, after which the second ligature is tied and the vein is divided. A hemostat is applied to each end beyond the ligature and transfixion sutures are inserted and tied. The deep femoral (profunda)

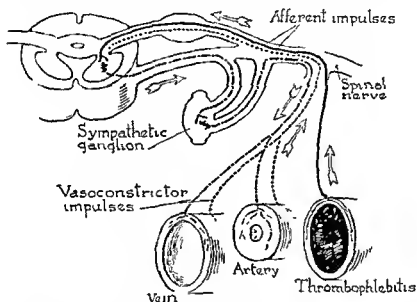


Fig. 30.—Diagrammatic representation of the mechanism of development of the clinical manifestations of thrombophlebitis. Impulses (depicted by arrow) originating in the thrombosed venous segment set up a vasomotor reflex resulting in generalized vasospasm of the involved extremity. (From Ochsner and DeBakey Arch Surg 40: 222, 1940.)

vein is inspected at its junction with the superficial vein; if the deep vein is also filled with clot, it is ligated close to the common femoral vein. The incision is closed, elastic bandages are applied from the toes to the knees, and active exercise of the legs, including walking, is begun as soon as possible. A blood transfusion may be of value if a significant amount of blood is lost or sucked out during the operation.

**Treatment of acute thrombophlebitis** is on a different basis. Acute thrombophlebitis is an inflammatory process pro-



ducing well-defined local and general symptoms. The commonest postphlebotic complication is obliteration of the common femoral and external iliac venous channels, with phlegmasia alba dolens (milk leg) resulting. Pulmonary embolism is a possibility, although an unlikely one, since the intravascular clot is firmly fixed to the inflamed intima.

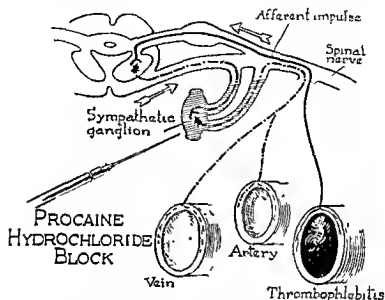


Fig 31.—Diagrammatic representation of the mechanism of relief of the clinical manifestations after procaine hydrochloride block in cases of thrombophlebitis. Block of the sympathetic ganglions with procaine hydrochloride interrupts the vasoconstrictor impulses and results in breaking of the vasomotor reflex (From Ochsner and DeBakey. Arch Surg 49: 272, 1946)

The usual methods of treatment are designed to decrease inflammation and increase venous drainage. Complete bed rest is instituted, with elevation of the affected limb at an angle of 30 degrees, and heat is applied either by means of a properly regulated heat tent or by hot wet packs from ankle to hip. Absolute immobilization of the leg is not advisable and the use of cold applications is contraindicated; such measures tend to decrease the rate of venous flow and to encourage progression of the inflammatory thrombosis. Penicillin may be administered, but the

effects of antibacterial drugs are inconstant at best. Ligation of the involved veins is quite contraindicated in the treatment of acute thrombophlebitis; the danger of pulmonary embolism is not great, and ill-advised operative interference may damage any femoral or inguinal venous and lymphatic channels not already involved in the inflammatory process.

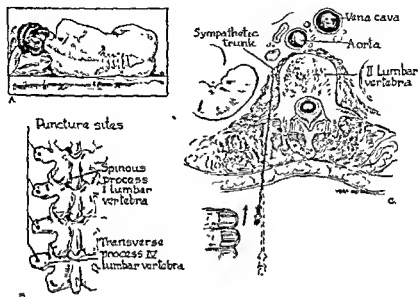


Fig 32.—Diagrammatic illustration of the technique of lumbar sympathetic block for thrombophlebitis of the lower extremity. A, Patient in the lateral recumbent position. B, Cutaneous sites of puncture, lying immediately over the transverse processes of the vertebrae. They may be determined by taking points approximately two and one-half fingerbreadths lateral to and on a horizontal level with the spinous processes of the first four lumbar vertebrae. C, Insertion of the needles. Each needle is inserted vertically until the transverse process of the vertebra, as shown by the dotted needle, is reached. The direction of the needle is then changed slightly toward the midline, and the needle is inserted approximately two and one-half fingerbreadths beyond the transverse process, so that its point lies near the anterolateral surface of the body of the vertebra, where the sympathetic chain lies. Five cubic centimeters of 1 per cent procaine hydrochloride solution is injected through each needle, care being taken to determine previously that the needle is not in a vessel. (From Ochsner and DeBakey. *Arch Surg* 40: 222, 1940.)

Procaine block of the lumbar sympathetic ganglia, strongly advocated by Ochsner and DeBakey,<sup>21</sup> is often of considerable value in acute thrombophlebitis, producing an acceleration of venous flow and relief of pain in the involved extremity. The rationale of regional sympathetic block in the treatment of thrombophlebitis is based upon the opinion, supported by clini-

cal and experimental evidence, that the thrombophlebitic process initiates a vasomotor reflex which produces a marked vasospasm of both the arterioles and the smaller veins. The consequent vascular occlusion may be so extensive that arteriolar pulsation in the affected area almost disappears. Repeated procaine block of the regional sympathetic ganglia will often cause rapid and effective relief of pain, subsidence of edema, and reduction of inflammation (Figs. 30 and 31). The procedure may be performed if necessary without moving the patient from his bed and requires no more anesthesia than an intracutaneous wheal of procaine, 1 per cent, at the site selected for introduction of the needle. A 20 or 22 gauge needle, 8 to 10 cm. long, is advised. The technique is illustrated in the diagram shown in Fig. 32. *The procedure, unless done quickly and expertly, is productive of some discomfort; a preliminary dose of morphine is helpful.*

Studies on the clinical use of tetraethylammonium bromide<sup>24,25</sup> appear to indicate that this drug partially blocks the autonomic ganglia, both sympathetic and parasympathetic, for a variable length of time. It may prove to be useful for releasing vasospasm and increasing blood flow to an extremity in the presence of thrombophlebitis, as an alternative measure to procaine block of the regional sympathetic ganglia. The value of this drug has not been definitely established at the present, clinical studies are still in progress.

### Pulmonary Embolism

One of the most tragic occurrences that may befall a surgical patient who has passed successfully through the early convalescent period is the sudden and totally unexpected development of massive fatal pulmonary embolism. Such an accident may occur without warning after an uneventful recovery when the patient begins to get up or even when he is preparing to go home. The complication is one which often cannot be foreseen or prevented, nor has any treatment which offers even a reasonable hope of success yet been devised.

Pulmonary embolism is a relatively common occurrence; it is responsible for approximately 6 per cent of all postoperative deaths and also for a high percentage of the instances of nonfatal pulmonary complications of the postoperative period. *Scv* does

not seem to be a contributory factor, although women are perhaps more frequently affected than men. Obesity appears to be a predisposing influence and pulmonary embolism is most common in subjects of the middle and upper age groups, practically all of the fatal cases occurring in patients past 40 and in most cases past 50 years of age. The type of operation has some bearing on the frequency of this complication; surgical procedures on the abdomen and pelvis, especially for malignant disease, and hernial repairs are more likely to be followed by pulmonary embolism than are operations in which no body cavity is entered. Patients with organic cardiac disease are also more often affected than those with normal cardiac function.

Phlebothrombosis, or quiet venous thrombosis, is probably the most common source of origin of the offending embolus, especially in surgical patients. Acute thrombophlebitis is less likely to be responsible, since the clot in a vein in which inflammation has developed is usually firmly adherent. Pulmonary embolism, in fact, may be the first evidence that venous thrombosis has developed in some area of the body. Chapman and Linton<sup>20</sup> have suggested that in patients with quiet venous thrombosis, straining or expiratory efforts with the glottis closed, as in use of the bedpan or in vigorous efforts to move about in bed, may act as the precipitating cause of embolism. Such efforts (Valsalva experiment) produce an increase in intrathoracic pressure and therefore an increase in venous pressure, together with obstruction to venous return. When the effort is released, the sudden drop in venous pressure and sudden emptying of the congested veins may result in embolism from an easily detached floating thrombus.

Symptoms of embolic occlusion of a pulmonary artery depend largely upon the size and number of the emboli. The condition frequently is not recognized at first because the signs and symptoms are not always characteristic and may be interpreted improperly. The first attack usually is not fatal; in most cases several minor embolic accidents, often unrecognized until after the diagnosis has become all too obvious, precede the terminal catastrophe. The complication is commonest within a period of seven to twenty days following operation.

The most characteristic indication of pulmonary embolism is the associated circulatory disturbance. A massive embolus which causes total obstruction of one or both pulmonary arteries usually is immediately fatal, the patient succumbing in profound shock, often syncopal in nature. Typically, he suddenly becomes weak and faint, the pulse becomes rapid and running, and the blood pressure falls abruptly. Pallor and sweating, as well as nausea or vomiting, usually appear. Severe but nonfatal emboli may be accompanied by peripheral vascular collapse of marked degree, and cyanosis and dyspnea also are frequently but not necessarily present. Less marked symptoms of a similar nature appear following the occurrence of pulmonary embolism in which the clots are smaller; in fact, the only symptom that may be present following the lodging of a small pulmonary embolus may be a sudden and somewhat persistent attack of faintness. If such a manifestation appears in the late postoperative period without an allocable cause, the possibility of pulmonary embolism should be strongly considered.

Nonfatal pulmonary emboli which produce areas of hemorrhagic pulmonary infarction may cause local signs and symptoms in addition to the general symptoms of collapse. Sudden pain in the chest may follow the lodging of the embolus, and cough, hemoptysis, and pleural pain sometimes appear after a short interval. An audible friction rub may be present after several hours, and evidences of pulmonary consolidation in the affected area sometimes can be detected upon physical examination. Roentgenologic examination occasionally shows an increased hilar shadow immediately after the lodging of the embolus, perhaps due to dilatation of the pulmonary conus and obstructed artery, but the typical wedge-shaped area of consolidation does not appear in the lung for a day or more. When the embolus is relatively small and the infarcted area is well supplied by collateral arterial branches, no evidence of any lesion may be present on physical examination, and the only indications of pulmonary embolism may be the *transient faintness* at the time of impaction of the clot, together with the moderate sustained rise in temperature and pulse rate over a period of several days.

Since there are no definite and diagnostic signs of minor pulmonary embolism and since the fatal attack usually is preceded by one or more minor embolic accidents, any occurrence during the

second or third week after a surgical operation which might resemble pulmonary embolism should be regarded as such and further embolic attacks anticipated.

Pulmonary embolism of minor degree is often erroneously diagnosed as postoperative pleurisy or pneumonia. A major embolic accident may also resemble acute coronary occlusion very closely, but certain characteristic points permit differentiation. Both are marked by the occurrence of sudden and severe shock, with pain in the chest, a subsequent rise in temperature, and leucocytosis.\* Embolism is more often accompanied by cyanosis and dyspnea; the pain is not often in the precordial region and is distinctly related to respiration. Coronary occlusion, on the other hand, is marked by severe and prolonged pain over the precordium, and a previous history of anginal pain can often be secured. However, a massive embolus may cause sufficient obstruction of the pulmonary artery to produce acute dilatation of the right ventricle and pulmonary conus, with increased pulsation visible over the corresponding area of the chest, and a loud systolic murmur, sometimes accompanied by gallop rhythm. Venous congestion at times may be present in the neck. Electrocardiographic changes accompanying pulmonary embolism may be diagnostic and differ from those usually seen accompanying coronary occlusion.

Much experimental work has been done<sup>11</sup> to determine the mechanism by which the embolic occlusion of a single pulmonary artery produces death, while operative ligation of the same vessel during the course of a pneumonectomy may be done with impunity. Diminution of circulating blood volume as a result of insufficient return of blood to the left heart from the lungs is the simplest explanation but is clearly inadequate. It is probable that the impact of the embolus in the pulmonary artery excites a reflex spasm of the vessel with consequent complete occlusion as well as reflex changes throughout the vegetative nervous system, with the production of shock, decreased systemic blood pressure, bronchial spasm, increased motility of the gastrointestinal tract, cardiac inhibition, and possibly constriction of the coronary vessels. The conclusion has been reached following experimental study that the widespread reflex changes occur as a result of sympathetic inhibition, many of the excitatory impulses traveling through the vagus nerves.

Prevention of pulmonary embolism offers more promise than does treatment. Routine prophylactic measures are directed chiefly toward prevention of venous thrombosis. When venous thrombosis (phlebothrombosis) does appear, either proper anticoagulant therapy, or emergency ligation of one or both superficial femoral veins, or both, is indicated at once. Even careful therapy of this type is not always entirely successful, however, since thrombosis may develop and progress with little clinical evidence. Lam and Hooker<sup>23</sup> believe that early postoperative ambulation is the most promising prophylactic measure available at present.

Treatment of the embolism itself depends first of all on the recognition of the condition; many times pulmonary embolism is diagnosed only at the necropsy table. Sudden cardiac failure, coronary occlusion, or pulmonary edema occurring without warning in the second or third postoperative week actually may be pulmonary embolism. Less severe attacks may be diagnosed as pneumonia or pleurisy, or simply as syncope.

Patients who have suffered a mild attack tentatively diagnosed as pulmonary embolism should be kept in bed. Immediate therapy is instituted to prevent as far as possible further embolic episodes. The choice of treatment depends upon the preferences of the surgeon; ligation of both superficial femoral veins with aspiration of the formed clot<sup>15</sup> may be done as an emergency procedure or anticoagulant therapy<sup>17, 22, 24</sup> with heparin or with heparin and dicumarol may be instituted immediately. If heparin is not instantly available, ligation is advisable without delay. Anticoagulant therapy alone probably is the method of choice when the thrombosis has extended to the iliac veins or the vena cava, with the single exception of suppurative pelvic thrombophlebitis. It is advisable also to begin anticoagulant therapy several hours after venous ligation in surgically treated patients to prevent formation of new clots or dislodging of old ones above the points of ligation.

The usual measures should be taken to prevent the development of constipation; a bland diet is given, with mineral oil and enemas as required. Moderate muscular exercise of the extremities may be continued to prevent extension of any thrombus that may be present. A severe embolic attack may be accompanied

by cyanosis and dyspnea; the asphyxia is best treated by administering oxygen in concentrations of at least 50 per cent at once and by continuing the use of the gas until dyspnea has vanished. Antispasmodic drugs are given as quickly as possible to decrease the reflex vascular spasm, and atropine is used to reduce the vagal overactivity and sympathetic inhibition. DeTakats and Fowler<sup>10</sup> advise the administration of papaverine, 0.03 Gm. (gr. 1/2), and atropine, 0.8 mg. (gr. 1/75), intravenously at once and suggest that the patient be watched closely for repeated emboli, the medication being given as frequently as indicated. Such medication is advisable even when the infarction is small, and the requisite drugs should be kept ready at the bedside of any patient who has had a minor embolic attack.

Other measures are probably of little use; pressor substances, which frequently also cause vagal stimulation, are not of much value. Morphine and morphine derivatives are contraindicated in treatment of pulmonary embolism because of their respiratory depressant action and occasional excitatory side effects. Digitalis is not applicable, since the mechanical defect is based upon pulmonary vascular obstruction. Nitrites are contraindicated in the presence of decreased blood pressure, and venesection also is entirely useless.

Although antispasmodic medication may be of some value in the treatment of major pulmonary emboli, in most cases the patient will succumb rapidly no matter what therapy is instituted. Proper treatment of pulmonary embolism is still based upon proper prevention and treatment of venous thrombosis (phlebothrombosis) and early recognition of premonitory attacks. The Trendelenburg operation for removal of clots has occasionally been advocated, but the disadvantages, impracticability, and high surgical mortality of the procedure are strong contraindications. Frequently, too, multiple small emboli may produce a clinical picture indistinguishable from that caused by a single massive embolus. In other cases the diagnosis may be mistaken and in still others the patient may have a better chance of surviving under conservative measures, which are unfortunately poor at best.



permit the spread of infected material to the subphrenic spaces behind the liver by means of the lymphatics accompanying the portal circulation. The organisms most commonly found include *Escherichia coli*, streptococcus, and staphylococcus.

Most infections of this area subside spontaneously and without the formation of pus, so that failure to diagnose the

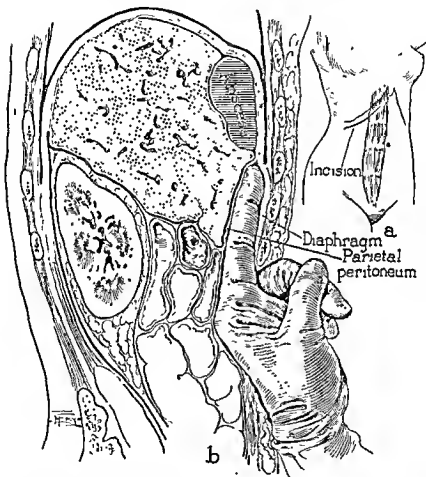


Fig. 35—Extraperitoneal drainage of an abscess in the right anterior superior space. As shown in *a*, an incision is made below and paralleling the right costal margin, passing through the flat abdominal muscles and the transversalis fascia. By means of the finger, the parietal peritoneum is peeled from the undersurface of the diaphragm until the abscess cavity is reached. The abscess is then drained extraperitoneally without contaminating either the pleural or the peritoneal cavity. (From Ochsner and Graves. *Ann. Surg.* 83:961, 1913, J. B. Lippincott Co.)

condition carries no serious consequences. In approximately one-third of the cases of subphrenic space infection, however, pus accumulates below the diaphragm, and proper diagnosis and surgical treatment are then necessary.

**Symptoms.**—The only dependable symptoms are the general ones characteristic of a suppurative focus somewhere in the body. As a rule, some antecedent intraperitoneal infectious process has already been treated, but the patient has failed to respond properly during the convalescent period. In a patient in whom continued fever, leucocytosis, tachycardia, and malaise persist for one or two weeks after the primary lesion has healed and exhaustive search has failed to reveal any evidence of disease elsewhere in the body, a subphrenic space infection is to be seriously considered. Although the onset of the disease may be acute and well defined when it is secondary to generalized peritonitis due to a perforated viscus, the picture presented is often diffuse, nonspecific, and gradually progressive.

**Localizing signs,** when present, consist of slight pain or difficulty on deep inspiration, felt vaguely in the right lower chest, and perhaps a sense of pressure, tightness, or slight pain in the right lumbar region. The diaphragm on the right side may be distinctly elevated late in the course of the disease, with a diminished respiratory excursion of the lung base, and the liver dullness may be increased, the liver edge sometimes being palpable on deep inspiration. Occasionally, mild tenderness to pressure over the twelfth rib may be present and may be the only noticeable sign. X-ray evidence is often lacking; when present, it may include elevation and respiratory immobility of the right half of the diaphragm, with obliteration of the costophrenic or cardiophrenic angle, and sometimes the presence of gas in the subphrenic space when an accumulation of pus has developed. *Lateral and anteroposterior roentgenograms should be secured with the patient erect.*

Late undiagnosed subphrenic abscesses may be responsible for the production of serous effusions in the adjacent pleural cavity or of empyema or pneumonitis. Such effects are not ordinarily seen when the diagnosis is made and the appropriate treatment instituted promptly.

Treatment of subphrenic space infections depends upon the stage of development of the disease. Simple supportive measures are instituted during the early period, since most infections in this area subside spontaneously. When the process has been present for two or more weeks and is continuing without improvement in spite of adequate antibacterial and general supportive therapy, surgical exploration is indicated, especially when local evidences suggest the presence of pus. Exploratory aspiration with a needle is never justified under any circumstances, since pus may easily be spread into the pleural cavity or into uncontaminated areas of the peritoneum. Operative exploration is relatively simple and may be performed under local or general anesthesia without shock to the patient.

The operative approach depends upon the location of the abscess, but no matter where the pus is located, it must be approached without entering either the pleural or the peritoneal cavities. Of the various operations which have been devised to avoid the spreading of contaminated material into uninvolved serous spaces, one of the safest is probably the procedure (Figs. 33, 34, and 35) advocated by Ochsner and Graves.<sup>21</sup>

### Parotitis

Parotitis is no longer a common postoperative occurrence; it is now seen in less than 0.1 per cent of surgical patients, but it still bears a high mortality rate.

Surgical infection of the parotid gland has no relation to epidemic parotitis (mumps), the infection is almost always staphylococcic in nature and is generally believed to gain access to the gland tissues by traveling from the mouth up along the parotid duct. The submaxillary glands are never involved by this type of inflammation, probably because their secretion is mucinous rather than serous and consequently is not favorable to bacterial growth. The complication is an exceptionally serious one in a surgical convalescent, not so much because of its own direct effect as because it usually occurs only in debilitated individuals and further decreases their chances for recovery. Dehydration and oral sepsis are predisposing factors.

Symptoms ordinarily appear abruptly within two to seven days after operation. The earliest manifestations are pain,

swelling, and tenderness over the affected parotid gland, with moderate dysphagia and with pain radiating to the ear. Fever is often marked (103 to 105° F.) and the pulse rate is elevated proportionately. Leucocytosis of variable degree is also present. The infection may progress very rapidly, with a marked increase in systemic toxic effects as well as in severity of local manifestations. The skin overlying the affected gland becomes tense, reddened, and shining, and the surrounding edema may spread down the neck and up the side of the face, sometimes closing the eyelids. Since the parotid gland contains many firm fibrous septa and has a dense fascial investment, little distention is possible and rapid necrosis and gangrene may occur before fluctuation can be noted. Treatment therefore should be instituted as soon as evidences of parotitis appear. Even though the gland may feel hard and brawny, thin pus sometimes can be milked from the opening of Stenson's duct, which is usually hyperemic and swollen.

**Prophylactic Measures.**—No prophylactic measures are required beyond those ordinarily taken in the preparation of the average surgical patient. Depleted fluids must be replaced and adequate fluid intake maintained following operation. The presence of oral sepsis should be noted before operation and appropriate measures taken to clean the mouth. Some authorities have advised against the use of atropine for any purpose following operation, since this drug depresses the salivary secretion. The use of chewing gum during the early postoperative period has been suggested to increase the flow of saliva.

**Treatment of surgical parotitis** should be instituted promptly. Conservative measures consist of the administration of the proper physiologic amounts of fluids and the use of hot packs or cold applications locally, according to the preference of the patient. Excellent results have been claimed for the use of deep x-ray therapy<sup>24</sup> and radium<sup>25</sup> applications, which must be administered, of course, by physicians trained in their use. After irradiation, no beneficial effects are noted for at least one day, and more commonly two. A decrease in general toxicity may be evident almost at once, however, even though inflammatory edema of the parotid region persists for a short while longer.

Sulfonamide drugs have proved to be of little value, but it is possible that penicillin in full dosage may serve as a highly useful therapeutic adjunct. Leithauser and Cantor<sup>35</sup> suggest the use of massive doses of Lugol's solution in treatment of acute secondary parotitis, with aspiration of pus if an abscess forms, but no surgical drainage. The drug is administered in doses of 20 minims every three hours during the day and night and is continued until the parotid infection has disappeared. These authors report use of this treatment in twenty-three patients with acute secondary parotitis with no deaths. Altemeier<sup>37</sup> has confirmed the therapeutic value of Lugol's solution in surgical parotitis and states that penicillin is also of considerable benefit.

If rapid improvement is not noted during such treatment, surgical measures should be adopted and must not be postponed more than two or three days following the onset of the disease in the expectation that fluctuation will develop. A longitudinal incision beginning 2 cm. anterior to the external auditory meatus and carried down to the fascia overlying the gland will avoid the facial nerve and Stenson's duct and yet give access to the infected areas. The incision should not extend through the fascia; the site of the infection may be located and drained by the insertion of a blunt clamp. One or two rubber dam drains should be left down to the infected region. Irrigation of the wound at intervals with normal salt solution or hydrogen peroxide may help to loosen any dried exudate. Hot wet packs are also of definite value.

Because *acute gastric dilatation* is so intimately associated with peritonitis, it is discussed under that heading instead of among the major postoperative complications.

### References

1. Coryllos, P. N.: Postoperative Pulmonary Complications and Bronchial Obstruction, *Surg., Gynec. & Obst.* 50: 795, 1930.
2. Driggs, R. D., and Deming, M. V.: Postoperative Atelectasis and Pneumonia. Diagnosis, Etiology, and Management Based Upon 1,240 Cases of Upper Abdominal Surgery, *Ann. Surg.* 121: 91, 1946.
3. Haight, C., and Ransom, H. K.: Observations on the Prevention and Treatment of Postoperative Atelectasis and Bronchopneumonia, *Ann. Surg.* 114: 243, 1941.

4. Eversole, U. H.: The Prevention and Management of Postoperative Pulmonary Complications, *S. Clin North America* 24: 515, 1944
5. Hunter, W. C., Krugier, J. J., Kennedy, J. C., and Sneed, V.: Etiology and Prevention of Thrombosis of Deep Leg Veins, Study of 400 Cases, *Surgery* 17: 178, 1945.
6. Bauer, G.: Heparin Therapy in Acute Deep Venous Thrombosis, *J. A. M. A.* 131: 196, 1946
7. Homans, J.: Deep Quiet Venous Thrombosis in Lower Limb, Preferred Levels for Interruption of Veins, Iliac Section or Ligation, *Surg., Gynec. & Obst.* 79: 70, 1944
8. Ochsner, A.: Venous Thrombosis, *J. A. M. A.* 132: 827, 1946.
9. Homans, J.: Medical Progress. Diseases of the Veins (concluded), *New England J. Med.* 235: 193, 1946.
10. deTakats, G., and Fowler, E. P.: Problem of Thromboembolism, *Surgery* 17: 153, 1945.
11. deTakats, G.: Heparin Tolerance Test, Test of Clotting Mechanism, *Surg., Gynec. & Obst.* 77: 31, 1943.
12. Allen, A. W., Linton, R. R., and Donaldson, G. A.: Venous Thrombosis and Pulmonary Embolism: Further Experience With Thrombectomy and Femoral Vein Interruption, *J. A. M. A.* 128: 397, 1945.
13. Barnes, A. R.: Pulmonary Embolism, *J. A. M. A.* 109: 1347, 1937
14. Gamble, H. A.: Prevention of Postoperative Embolism and Phlebitis, With Description of Apparatus Employed, *Am. J. Surg.* 28: 93, 1935.
15. Allen, A. W.: Interruption of the Deep Veins of the Lower Extremities in the Prevention and Treatment of Thrombosis and Embolism, *Surg., Gynec. & Obst.* 81: 519, 1947.
16. Murray, G. D. W., and Best, C. H.: Use of Heparin in Thrombosis, *Ann Surg.* 108: 163, 1938
17. Murray, G.: Anticoagulants in Venous Thrombosis and the Prevention of Pulmonary Embolism, *Surg., Gynec. & Obst.* 81: 665, 1947.
18. Loewe, L., Rosenblatt, P., and Hirsch, E.: Venous Thromboembolic Disease, *J. A. M. A.* 130: 386, 1946.
19. Loewe, L. and Hirsch, E.: Heparin in the Treatment of Thromboembolic Disease, *J. A. M. A.* 133: 1263, 1947.
20. Barker, N. W., Cromer, H. E., Hurn, M., and Waugh, J. M.: Use of Dicumarol in Prevention of Postoperative Thrombosis and Embolism With Special Reference to Dosage and Safe Administration, *Surgery*, 17: 207, 1945.
21. Evans, J. A., and Boller, R. J.: The Subcutaneous Use of Heparin in Anticoagulation Therapy, *J. A. M. A.* 131: 879, 1946.
22. Allen, E. V.: The Emergency Treatment of Vascular Occlusion, *J. A. M. A.* 135: 15, 1947.
23. Fine, J., and Starr, A.: Surgical Therapy of Thrombosis of Deep Veins of Lower Extremities, *Surgery*, 17: 232, 1945.
24. Moses, W. R.: Ligation of the Inferior Vena Cava or Iliac Veins, *New England J. Med.* 235: 1, 1946.

25. Collins, C. G., Nelson, E. W., Jones, J. R., Weinstein, B., and Thomas, E. P.: Ligation of the Vena Cava, *New Orleans M. & S. J.* 99: 488, 1947.
26. Allen, A. W., Linton, R. R., and Donaldson, G. A.: Venous Thrombosis and Pulmonary Embolism, *J. A. M. A.* 133: 1268, 1947.
27. Ochsner, A., and DeBakey, M.: Therapy of Phlebothrombosis and Thrombophlebitis, *Arch. Surg.* 40: 203, 1940.
28. Berry, R. L., Campbell, K. N., Lyons, R. H., Moe, G. K., and Sutler, M. R.: The Use of Tetraethylammonium in Peripheral Vascular Disease and Causalgic States, *Surgery* 20: 525, 1946.
29. Coller, F. A., Campbell, K. N., Berry, R. E. L., Sutler, M. R., Lyons, R. H., and Moe, G. K.: Tetra-Ethyl-Ammonium as an Adjunct in the Treatment of Peripheral Vascular Disease and Other Painful States, *Ann. Surg.* 123: 729, 1917.
30. Chapman, E. M., and Linton, R. R.: Mode of Production of Pulmonary Emboli, *J. A. M. A.* 129: 196, 1945.
31. deTakats, G., Beck, W. C., and Fenn, G. R.: Pulmonary Embolism; Experimental and Clinical Study, *Surgery* 6: 339, 1939.
32. Lam, C. T., and Hooker, D. H.: Pulmonary Embolism. A Statistical Study, With Particular Reference to the Value of Certain Preventive Measures, *Ann. Surg.* 123: 221, 1946.
33. Ochsner, A., and Graves, A. M.: Subphrenic Abscess; Analysis of 3,372 Collected and Personal Cases, *Ann. Surg.* 98: 961, 1933.
34. Hare, H. F.: Management of Acute Postoperative Parotitis, *S. Clin. North America* 24: 603, 1944.
35. Buschke, F., and Cantril, S. T.: Course of Postoperative Parotitis Under Radiation Therapy, *West. J. Surg.* 52: 21, 1944.
36. Leithauser, D. J., and Cantor, M. O.: Massive Doses of Lugol's Solution in Acute Secondary Parotitis, *Ann. Surg.* 111: 650, 1940.
37. Altemeier, W. A.: Acute Secondary Parotitis, *Surgery* 20: 191, 1946.
38. Evans, J. A., and Dee, J. F.: Anticoagulant Treatment of Postoperative Venous Thrombosis and Pulmonary Embolism, *New England J. Med.* 238: 1, 1948.
39. Parker, T. W., and Kvale, W. F.: Neutralization of Heparin With Protamine (Salmine), *J. Lab. & Clin. Med.* 32: 1396, 1947.

## CHAPTER 14

# INTESTINAL OBSTRUCTION AND PERITONITIS

### Mechanical Intestinal Obstruction

The average patient convalescing from a laparotomy experiences a temporary paresis of the intestinal tract as a result of trauma to the bowel and to the peritoneum during the operation. Normal peristaltic activity of the intestine is resumed ordinarily within one or two days after recovery from anesthesia, and the nausea, vomiting, and paralytic distention of the small bowel disappear with the restoration of proper motor activity. Sometimes, however, the functional intestinal paralysis may persist for several days and may merge progressively and deceptively into actual intestinal obstruction.

Differentiation between prolonged postoperative paresis of the bowel and early mechanical intestinal obstruction is not always easy at this critical period. The surgeon naturally is unwilling to submit the convalescent patient to an unnecessary second operation and perhaps may wait until the presence of mechanical obstruction becomes clinically obvious. Probably the chief reason for the high mortality of acute postoperative intestinal obstruction is that therapy is instituted too late in the course of the disease, and irreparable damage has been permitted to occur to the bowel wall before the significance of the symptoms has become unmistakable. For this reason Morgan and Henderson<sup>1</sup> have urged that a consultation by a second surgeon, unfamiliar with the case and consequently unprejudiced and objective in judgment, be secured as soon as it is apparent that the postoperative intestinal paresis is lasting longer than the usual one to three days or is more than ordinarily severe. Intestinal obstruction, especially in the postoperative patient, is one of the most feared of all surgical complications since early identification is so difficult and since each hour's delay adds so greatly to the mortality.

**Etiology.**—Mechanical obstruction, like functional intestinal paresis, originates chiefly as a result of trauma to the ab-



dominal contents during operation. There are three main contributory causes in the ordinary *uninfected case*—(1) Manipulation of the bowel and traction upon the mesentery produce a temporary disturbance in innervation of the musculature. (2) Irritation of the serous coat of any of the abdominal viscera causes a roughening of the peritoneum and a consequent local outpouring of fibrinous exudate. (3) Failure to reperitonize raw surfaces resulting from the operative procedure encourages the development of fresh adhesions between bowel or omentum and the traumatized area. Adoption of a gentle and meticulously careful operative technique therefore will minimize the danger of postoperative intestinal obstruction from these causes, which cannot be entirely avoided in any operative procedure.

The development of peritoneal adhesions is a basic factor in the progress of healing following operative procedures within the abdomen. All operations upon the gastrointestinal tract, for example, depend for their success upon the rapid formation of a smooth peritoneal coat over the area of surgical repair. Some individuals, however, exhibit a tendency to develop massive and widespread peritoneal adhesions out of all proportion to the extent of the operation performed. Mechanical obstruction as a result of the formation of bands or kinks consequently may appear after even a relatively minor intra-abdominal operation. Obstruction of this type probably is commonest following appendectomy and may appear in clean cases as well as in those exhibiting peritoneal irritation and infection. Efforts have been made to prevent the excess formation of adhesions in the patient convalescing from a laparotomy by leaving such materials as amniotic fluid concentrate or papain in the abdominal cavity when the incision is closed, if there is no local contraindication, but no conclusive clinical proof has been advanced that these substances are of value. The use of heparin for this purpose has been advocated in selected cases but is not generally accepted.<sup>2</sup>

Wangensteen<sup>3</sup> has stated that "... obstructions in the early convalescent period are largely brought about by the collection of fluid and gas in a bowel whose motility is impaired. Whereas, when empty such a gut may not readily be obstructed, when heavy because of lack of absorption of the large quantity of fluids normally dumped into it, a few fibrinous adhesions may

readily block its continuity." For this reason, the prevention of intestinal distention during early convalescence will decrease the likelihood of development of mechanical obstruction.

**Pathology.**—Peritoneal adhesions may vary in size and extent from the long filamentous form to the dense sheets and masses of fibrin which sometimes are seen following peritonitis. The location of the adhesion is more important than its size; a tiny plastic band occasionally may produce complete obstruction in a patient with functional paresis of the bowel, although massive bands and sheets of adhesions may exist in another individual without any interference to the progress of intestinal peristalsis.

**HIGH OBSTRUCTION**—Since the function of the upper small intestine is digestive and that of the lower small bowel is absorptive, the pathologic physiology and the clinical course of intestinal obstruction vary with the location of the block. High obstruction usually is simple in type. Since there is little retention of fluid, no closed loops develop, and the pathologic effects are due chiefly to the obstruction to flow of intestinal contents into the absorptive region of the ileum. Approximately 7 liters of digestive fluids are poured into the upper small bowel normally each day and are reabsorbed in the lower bowel. Obstruction to the lumen of the small bowel causes regurgitation of the fluid into the stomach and loss by vomiting, which develops early in high obstruction and soon becomes profuse and almost continuous. With the loss of chlorides in the vomited gastric and duodenal secretions and the decrease in urinary output, there occurs a concomitant drop in chloride content of the blood and a rise in nonprotein nitrogen. Collier and Maddock<sup>4</sup> have estimated that loss of body fluid equivalent to 6 per cent of the body weight will result in marked and clinically apparent dehydration. Since fluid loss of this magnitude may occur in one or two days' time in jejunal obstruction, the urgency of the problem of fluid replacement in intestinal obstruction is evident.

**OBSTRUCTION IN THE LOWER ILEUM.**—Obstruction in this area of the small bowel is more common; a high percentage of cases of postoperative mechanical obstruction follows appendectomy and pelvic operations. In such a case nausea and vomiting may not appear until relatively late in the course, since some re-

absorption may occur in the early stages and since there is a larger area of bowel to act as a reservoir for the retention of fluid. There is consequently less early fluid and electrolyte loss and less alteration in the components of the blood, but there is correspondingly greater danger of strangulation. The collection of fluid and swallowed air in the loops of intestine just above the point of obstruction may produce an increasing distention which, if unrelieved, will cause a buckling or kinking of the affected segments of bowel just as the partially inflated inner tube of an automobile tire will buckle if it is bent.

The development of one or more closed loops of this type will prevent the emptying of the affected area of bowel, even by regurgitation, especially after peristalsis becomes subnormal and weak. As accumulation of fluid and gas in atonic segments of the small bowel continues, circulatory disturbances of the intestinal wall develop as a result of the unrelieved intraluminal pressure. The integrity of the intestinal mucosa soon becomes impaired and toxic products of intestinal putrefaction, which do not pass through the normal mucosa, are absorbed into the blood stream with the subsequent appearance of clinical signs of systemic toxemia. At first simply edematous and congested, the stretched and distended bowel rapidly becomes cyanotic as the pressure within the lumen increases to the point where venous drainage is blocked. Plasma is lost by transudation across the damaged mucosa into the lumen of the obstructed bowel. Hemorrhagic areas appear, usually at first on the antimesenteric border where the circulation is normally poorest, and finally infarction and gangrene of the entire obstructed area complete the pathologic picture. The degree of circulatory change in the bowel wall is directly proportional to the degree of distention, the quantity of contained fluid, and the duration of the disease. If closed loops do not develop, strangulation does not appear and the clinical picture is simply that of dehydration and electrolyte imbalance.

The most important factor in the physiopathology of high obstruction of the small intestine therefore is the fluid and electrolyte loss, while the lethal effect of low small bowel obstruction is due primarily to strangulation of bowel wall and absorption of toxic intestinal products. Fluid and salt loss is a secondary contributory factor in the course of progressive ileal obstruc-

tion; reabsorption of intestinal fluids continues for a short time, but accumulation in the obstructed bowel soon begins to take place and profuse vomiting may be a still later manifestation. The nature of the toxin absorbed from the closed bowel loop has been studied for some time. It was originally believed that a new and highly poisonous product was elaborated in the strangulated loop. The current opinion, however, is that the toxic material is not a substance peculiar to intestinal obstruction but consists simply of the bacterial products ordinarily found in the intestinal tract, which, while not absorbed into the blood stream through the intact mucosa, pass readily through mucosa damaged by strangulation. Loss of plasma across the damaged bowel wall into the lumen also contributes to the shocklike picture that accompanies advanced complete intestinal obstruction.

**Diagnosis.**—Mechanical intestinal obstruction is commonly stated to be a syndrome consisting of abdominal pain, vomiting, distention, and obstipation. Although these manifestations are characteristic, they may not appear until late in the course of the disease, when it has progressed beyond the point at which successful intervention is possible. Efforts therefore must be made to detect and to evaluate the earliest possible evidences which might suggest the presence of intestinal obstruction.

The first signs of obstruction usually appear within four to eight days following operation, when peristaltic function is beginning to return. The patient's general condition and clinical appearance may be perfectly satisfactory at the time of onset of obstruction. Undue persistence of nausea and vomiting and the presence of colicky pains synchronous with the occurrence of audible borborygmi are the earliest manifestations of small bowel obstruction and should suggest the possibility. Recognition of the significance of intestinal colic at this period is of the greatest importance. Auscultation of the abdomen will demonstrate that the recurrent cramping pain of which the patient complains is synchronous with the appearance of audible borborygmi and that the colic and the intestinal gurgling are proportionate in intensity. Earlier recognition and more effective treatment of postoperative intestinal obstruction will be achieved by frequent and careful auscultation of the abdomen in patients who are suffering a stormy postoperative convalescence with

prolonged disturbance of gastrointestinal function. No sedatives are to be given for abdominal pain in such patients; the diagnostic significance of intestinal colic is lost thereby and delay in recognition of mechanical obstruction will result; moreover, pain of this type is not relieved for any length of time by sedatives.

Slight distention may or may not appear within eight to twelve hours after the development of obstruction, depending upon the amount of gas present in the bowel. Abdominal distention is not a dependable early sign of obstruction; it may not appear until late in the course of the disease. Intestinal colic, however, is significant and marked in the early hours, and loss of appetite and nausea are present even though vomiting may not yet be apparent. At this stage the clinical appearance of the patient is deceptively good, although the pulse rate and the leucocyte count may be beginning to rise. There is often no significant change in the temperature until late in the course of obstruction.

As time passes the general appearance of the patient begins to change in proportion to the type, degree, and duration of the obstruction. High obstruction with marked fluid loss as a result of copious vomiting will produce dehydration quickly and the pulse rate will rise rapidly. Restoration of depleted fluids and electrolytes will bring about rapid improvement in the general condition. The clinical improvement is independent of local alterations in the bowel wall and does not permit further postponement of operation. Low ileal obstruction without marked loss of fluid produces little change in general condition until closed loops develop and strangulation begins. The onset of circulatory damage to the bowel by sudden acute strangulation, as in strangulated hernia, is marked by severe continuous pain, marked local tenderness, and rapid deterioration of general condition; the progression of simple obstruction to strangulation in intestinal block due to postoperative adhesions, however, may be marked only by a slow continuous rise in temperature, pulse rate, and leucocyte count, although the patient becomes anxious and restless and experiences an increase of pain and tenderness in the region of the strangulated loops. At this time, too, the vomitus usually becomes more profuse.

Later, as the strangulation becomes more advanced, a peritoneal exudate develops and well-defined abdominal pain appears, no longer cramplike but more constant in nature. Tenderness to pressure and rebound tenderness may be elicited and are of great significance. When the bowel wall has completely lost its viability and gangrene has begun, hemorrhage into the lumen may occur and may help to aggravate the effects of the toxemia in producing the shocklike picture characteristic of intestinal strangulation, marked by a rapid running pulse, profound toxicity, and complete prostration. In the terminal stages, when the patient is moribund, the vomitus becomes profuse and foul smelling ("fecal").

One of the most reliable aids to early diagnosis of obstruction is the *plain x-ray* picture of the abdomen, which will often show the characteristic changes in the intestine more quickly and more dependably than physical examination, since gas is visible roentgenologically before distention is clinically evident in the abdomen. Under normal circumstances the gas in the small bowel is mixed diffusely with the fluid content so that none can be seen upon x-ray examination. The presence of visible gas in the small intestine therefore is direct evidence of abnormal intestinal stasis, except in patients who have recently taken powerful cathartics or who have acute gastroenteritis and in children under 3 years of age, who may exhibit gas in the small bowel normally.

Roentgenologic examination of the abdomen should be made as soon as the earliest signs suggestive of postoperative intestinal obstruction are noted. Barium should never be given by mouth, since it cannot pass the obstructed loop and is too heavy to be regurgitated. Barium administered by enema is useless from a diagnostic standpoint, for the ileocecal valve will impede its entrance into the small intestine. Plates should also be made with the patient erect whenever possible in order to demonstrate the presence of fluid levels. If he is too ill to be moved from the supine position, an anteroposterior exposure may be made with a vertical beam to show the presence of gas and a lateral exposure with a horizontal beam to demonstrate fluid (Fig. 36). This diagnostic measure is of the greatest value, and satisfactory pictures can be secured with a portable x-ray machine without moving the patient from his room.

The earliest evidence of intestinal obstruction consists of the presence of irregular areas of gas in the center of the abdomen (Fig 37). As the accumulation increases, distention of the bowel may become evident, often with characteristic formation of a herringbone pattern as the result of the flattening of the valvulae conniventes (Kerkring's folds). Such a picture is definitely diagnostic of intestinal obstruction and demands emergency operation.

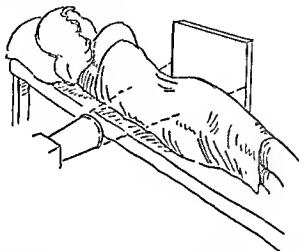


Fig 36 —Correct lateral position for roentgenogram to demonstrate possible fluid levels in the obstructed bowel in suspected intestinal obstruction. Fluid levels can be demonstrated also in the upright position but not by flat plates, in which only gas can be demonstrated.

If the quantity of gas present is relatively small and is diagnostically inconclusive, roentgenograms should be repeated every two hours until the diagnosis can be made or excluded by examination of the series of successive plates. Gas noted in the colon on the first film should be removed by means of an enema before the second picture is made. Reappearance of gas in the colon indicates that the block, if present, is incomplete; absence of gas from the colon and increase of gas in the small bowel indicate the existence of a complete obstruction. In general, the lower the obstruction is located in the small intestine, the greater the quantity of gas and fluid that is retained. As the obstruction advances, increasingly large quantities of gas and fluid

accumulate, with well-defined fluid levels. The degree of distention of the bowel is of great significance, a marked degree presaging strangulation.



Fig. 37 —Roentgenologic demonstration of early intestinal obstruction. The small bowel is distended, but no fluid levels are present.

When strangulation is unmistakably present, as evidenced by localized tenderness, rebound tenderness, or untoward changes in the patient's general condition, with a steady rise in temperature, pulse rate, and white blood cell count, immediate operation is necessary and already has been delayed too long. By this time, advanced distention and edema of the bowel wall may have impaired its contractility; colic and borborygmi then disappear and secondary paralytic obstruction supervenes. The abdomen may then be perfectly silent to auscultation.



In *summary*, the presence of increasing intestinal colic after the third or fourth postoperative day, with or without frequent and copious vomiting and gastric retention, indicates the probability of a mechanical obstruction of the small bowel. Frequent examinations of the patient should be made, with repeated auscultation of the abdomen, and flat and vertical roentgenograms of the abdomen should be secured after an enema has been administered. The mortality of mechanical intestinal obstruction is without question the mortality of delay; much more harm is done by waiting until the diagnosis is unmistakable than by operating too early on an occasional patient who may not need an operation. This fact has been particularly emphasized by Stone and Owings,<sup>6</sup> who report a series of twenty-seven consecutive patients with acute small intestinal obstruction, all treated by immediate operation, with only two deaths.

**Treatment.**—The only proper therapy of complete mechanical obstruction is surgical; all other measures are simply adjuncts employed to prepare the patient for operation, to prevent the progress of the obstruction, or to diagnose the site and type of the lesion. Even though the patient may not appear acutely ill, no time should be lost in releasing the obstructed bowel once the diagnosis has been made. The chief aims of treatment include relief of distention, correction of disturbed fluid and electrolyte balance, release of obstruction, and restoration of normal function. The use of peristaltic stimulants of any kind is absolutely contraindicated when intestinal obstruction is suspected.

**PROPHYLACTIC MEASURES.**—Prophylactic measures are always instituted in any convalescent patient if functional paresis of the bowel appears to be unduly prolonged after operation and if it is suspected that intestinal obstruction may develop. Efforts are made to reduce distention and to replace depleted fluids and electrolytes, while frequent examinations of the patient's abdomen are made by auscultation and roentgenography.

Probably the most widely used prophylactic measure is *constant gastroduodenal suction by means of the Wangenstein apparatus*. A Levin tube is passed through the patient's nose (p. 321) and into the stomach and duodenum and is then connected to a siphonage apparatus which exerts a constant suction of about 75 cm. of water (Fig. 18). The tube is perforated

for the distal ten inches so that effective drainage of both the stomach and the duodenum can be secured. Usually, the tip of the catheter will enter the duodenum without difficulty; its passage beyond the pylorus will be encouraged if the patient takes sips of water and is placed on his right side. The nature of the aspirated fluid is noted and the quantity recorded.

Replacement of fluid and electrolytes must follow a planned program while gastroduodenal suction is being employed. The quantity of fluid aspirated from the patient's gastrointestinal tract is charted and the daily total drainage computed. This lost fluid is replaced by administration of a similar quantity of fluid parenterally in addition to the basic amount required to maintain water balance. Since the fluid lost from the upper alimentary tract is lower in salt content than normal salt solution, the replacement fluid is made up of equal parts of normal salt solution and of dextrose (5 per cent) solution. For example, if a patient requires a daily intake of 2,500 c.c. of fluid parenterally to assure a daily urinary output of 1,000 to 1,500 c.c. and if 1,000 c.c. of fluid is lost by gastrointestinal suction, the fluid intake should amount to 3,500 cubic centimeters. Since 1,000 c.c. of normal salt solution usually satisfies the daily sodium chloride requirement and since half the amount lost by suction is to be replaced by normal salt solution, the fluids used in this hypothetical case will consist of 1,500 c.c. of normal salt solution and 2,000 c.c. of dextrose (5 per cent) solution. Of course, any fluids given by mouth and recovered in the suction drainage are deducted from the total amount of drainage charted.

The patient's chest should be examined daily to note any signs of incipient pulmonary edema, and the general body tissues should be inspected to detect early evidences of fluid retention. Blood chemistry studies are secured daily until the electrolyte balance has returned to normal.

The return of peristaltic function in the intestine may be detected without difficulty when the patient's clinical condition begins to improve. One or two hundred cubic centimeters of fluid are given orally and the tube is clamped off for two hours; if the quantity of fluid recovered by aspiration at the end of that period is less than that originally introduced, intestinal motility is beginning to reappear. At this time also, gas is passed per rectum.

Although the gastroduodenal suction apparatus is of great value in prevention of intestinal obstruction and relief of upper intestinal distention, there has been considerable discussion concerning its safety as a form of actual treatment in ileal obstruction. Wangenstein<sup>1</sup> points out that if suction drainage is instituted, no systemic changes in the patient's condition will occur as long as nutrition of the bowel wall remains unimpaired and fluids and electrolytes are supplied in proper amounts. If simple obstruction is present, he believes that the progress of the condition may be followed safely by frequent auscultatory and x-ray examination of the abdomen. If roentgenologic evidence of distention persists and the stasis is unrelieved after forty-eight to seventy-two hours of nonoperative treatment, then surgical relief of the obstruction is indicated, even though no untoward change has occurred in the patient's condition. Management by this method requires extensive experience in the diagnosis and treatment of mechanical intestinal obstruction as well as the ability to recognize the signs and symptoms of intestinal strangulation in its earliest stages.

The use of suction drainage should never be permitted to delay operation when a definite intestinal block is present. Since the apparatus can drain only the stomach and upper small bowel, kinked closed loops may still develop near the point of obstruction with subsequent strangulation, even though the suction apparatus may be functioning perfectly. While gastroduodenal suction is invaluable as a prophylactic or supportive measure therefore, it is potentially too dangerous to use as a form of conservative or delaying treatment after complete mechanical intestinal obstruction has developed. Immediate operation as soon as the diagnosis is reasonably certain is preferable to waiting for signs of progression of intestinal damage under nonoperative treatment. In every case of obstruction, operation should be preceded by insertion of a gastric drainage tube, aspiration of gastric contents, lavage of the stomach, and institution of constant suction drainage to be continued before, during, and after operation.

Use of the *Miller-Abbott tube*<sup>2</sup> is advocated widely in prophylaxis and treatment of intestinal obstruction of certain types. This apparatus affords a practical and safe method for nonoperative drainage of the entire small bowel down to the actual

site of obstruction or even to the ileocecal valve. The Miller-Abbott tube is of particular value under the following circumstances:

1. Treatment of paralytic intestinal obstruction (adynamic ileus); for example, in association with spreading or generalized peritonitis.

2. Prophylaxis against the development of paralytic intestinal obstruction in early peritonitis or of mechanical obstruction in the early postoperative period. Operations in which considerable handling of the bowel is necessary or in which large areas of raw nonperitonized surfaces are left are likely to be followed by development of plastic and fibrinous adhesions which later may produce mechanical intestinal obstruction. Prophylactic use of the Miller-Abbott tube during the first few days after operation will help to prevent such a complication.

3. Treatment or preparation for operation of a patient with incomplete mechanical intestinal obstruction. In incomplete obstruction, some passage of fluid and gas into the colon continues and strangulation is less likely. Progressive distention of the partially obstructed loops can occur, however, with development of complete obstruction at any time without warning. Suction drainage of the bowel proximal to the point of incomplete obstruction often will relieve distention and restore normal function. The diagnosis of incomplete obstruction must be definite if the Miller-Abbott tube is to be used as a method of treatment or even of delaying operation. Close watch must be maintained both by clinical and radiologic observation to insure immediate recognition of complete intestinal obstruction.

4. Protection of sutured bowel against distention during the early postoperative period. Intestinal anastomoses, even those in the colon, may leak or even break down if tension develops before healing is well under way. Gastroduodenal suction with a Levin tube is sufficient following operations on the small bowel, but the use of a Miller-Abbott tube passed to the lower ileum is advocated in some clinics<sup>7,8</sup> following resection of the right colon. This practice is not general, simple suction drainage of the stomach when necessary being the usual method.

5. Preoperative deflation of the small bowel when extensive resections of the colon are contemplated. Passage of a Miller-Abbott tube to the lower ileum before colectomy for such

conditions as ulcerative colitis or multiple polyposis of the colon will permit easy retraction of the small bowel, closely pleated upon the tube, away from the field of operation, greatly facilitating the procedure. The tube then may be allowed to remain

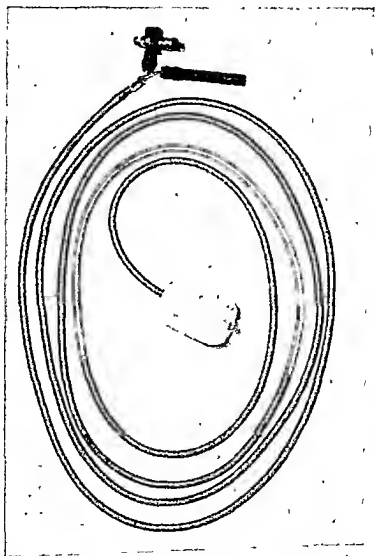


Fig 38—Miller-Abbott tube. The tube has a double lumen throughout its entire length, the smaller leading to the interior of the balloon and the larger serving for suction drainage.

for two or three days after operation to minimize distention and discourage the development of adhesions

6. Prophylaxis against distention following such operations as repair of large ventral hernias<sup>9</sup> in which distention alone may cause impaired wound healing or even dehiscence

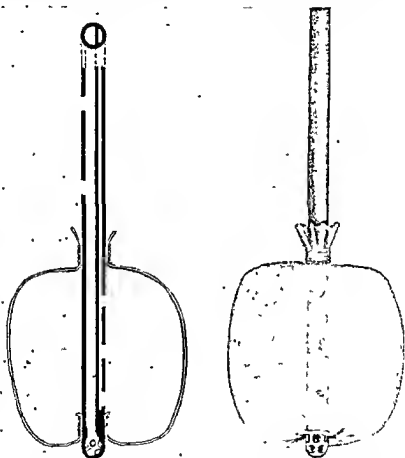


Fig. 39 —Miller-Abbott tube diagram of construction. Smaller lumen is for inflation and deflation of balloon, larger lumen opens in small metal tip. Neither channel connects with the other.

Within these limits, the Miller-Abbott tube is a useful and valuable apparatus. If used improperly to accomplish a purpose for which it is not intended, as, for example, in treatment of complete obstruction of the colon or lower ileum, the double-lumen tube may prove more dangerous than beneficial.

to active regurgitation of fluid into the stomach, with strong reverse peristalsis, the best plan is to allow the proper short length of tubing to remain in the stomach with the balloon deflated, continue gastric suction, and keep the patient on his right side as much as possible. As the regurgitation diminishes, the prospect of passage of the tube increases. In some cases,



Fig. 40 — Miller-Abbott tube at pylorus (small bowel obstruction).

introduction of several cubic centimeters of water into the balloon may encourage its passage into the duodenum. Use of special weighted tips has been suggested to increase the likelihood of prompt passage through the pylorus; for example, the introduction of mercury into the balloon (Smith,<sup>4</sup> Cantor,<sup>12</sup> Harris<sup>13</sup>). Such special methods probably are of most value to

those with wide experience in passage of the double-lumen tube and may only add to the difficulties of those who use it less often.

The tube is marked at six-inch intervals so that its descent may be followed; if swallowed too rapidly, it will coil in the stomach. In the average case, the tube may be passed into the



Fig. 41 — Miller-Abbott tube in duodenum (small bowel obstruction). The balloon is inflated immediately after the tube has passed the pylorus

nose at a rate of two inches (5 cm.) every twenty to thirty minutes. Advance is much slower in the presence of obstruction or distention; in paralytic ileus the tube may advance only an inch in several hours, as the distended atonic bowel slowly recovers contractility following decompression. Since the bowel virtually pleats itself along the tube, the entire small bowel from



pylorus to cecum can be drained although the length of tube passed beyond the pharynx amounts to only ten feet. Introduction of a small amount of barium in dilute suspension may be used to determine the site and nature of the obstruction.

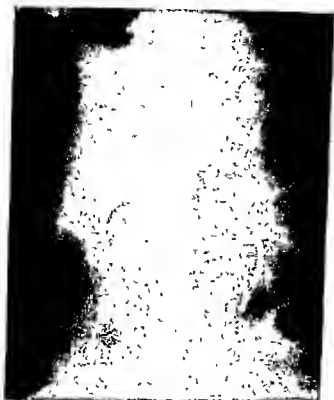


Fig. 42.—Miller-Abbott tube in ileum (almost complete relief of small bowel distention)

In general, this tube may be allowed to remain in place for several days if necessary, with the employment of constant suction drainage. Occasionally, distention of the stomach will occur after the Miller-Abbott tube has reached the lower ileum and will require aspiration by a small Levin catheter passed to the stomach through the other nostril. Each day or two the double-lumen tube should be pulled out of the nose for a distance of several inches and the local accumulation of mucus removed,

after which the tube is replaced as before. Instillation of Butyn or Nupercaine solution into the nostril at intervals may help relieve irritation. Removal of the tube when no longer needed is accomplished simply by deflation of the balloon and gentle withdrawal over a period of several hours, one or two inches at a time.



Fig 42—Miller-Abbott tube at ileocecal valve (relief of obstruction of small bowel, as demonstrated by introduction of a small amount of thin barium suspension)

*Other conservative methods* are used to assist the return of peristalsis and to overcome prolonged intestinal distention. A heat tent may be placed over the abdomen and the patient placed in Fowler's position to insure ease of respiration and relaxation of the abdominal wall. Enemas, still used occasionally, obviously are of no value in treatment of complete mechanical

intestinal block. Pure oxygen may be administered constantly by means of a Boothby or a Barach mask; neither a tent nor an intranasal catheter will suffice. The use of pure oxygen in patients suffering from intestinal distention has been advocated by Fine and associates<sup>14</sup> because of the decreased vital capacity induced by the presence of abdominal distention and because the decrease in partial pressure of nitrogen in the alveolar air when pure oxygen is breathed will tend to encourage the absorption of nitrogen from the intestinal gases into the blood stream and therefore will actually diminish gaseous distention (p. 806). Finally, patients who show evidences of strangulation are helped by transfusions of blood to replace the plasma and whole blood lost into the affected bowel segments.

**PREOPERATIVE PREPARATION.**—Much time may be saved if, in patients who require operation for intestinal obstruction, at the outset of treatment a Miller-Abbott tube is employed rather than a gastroduodenal tube which later may have to be replaced by the double-lumen tube. Even if the double-lumen tube remains proximal to the pylorus, it will work as efficiently with constant suction as the Levin catheter, while if the tip is successfully passed into the duodenum after several hours, the balloon may be inflated and the tube allowed to progress down the bowel. Just as in the case of the Wangenstein suction apparatus, however, the double-lumen tube is not to be used alone for treatment and should not be permitted to delay operation when there is evidence that the vitality of the bowel wall is impaired. Operation is then the only possible procedure. Probably the chief contraindications to the use of nonoperative methods of intestinal decompression are the false sense of security that is afforded, the tendency to defer operation dangerously long when the patient begins to show temporary improvement, and the length of time required to drain the obstructed area successfully.

When the patient is obviously in good condition, obstruction is of short duration, and no evidence of strangulation is present, several hours may perhaps be spent in an effort to pass the Miller-Abbott tube into the intestine and to relieve the progressive distention. When obstruction is of relatively long duration, the patient's general condition is deteriorating, and strangu-

lation is possible, only enough time should be spent before emergency operation to administer the necessary supportive measures and to empty the stomach. In such a case, peristalsis is irregular, the small bowel is distended, atonic, and edematous, and many hours may be spent in vain attempts to pass the Miller-Abbott tube beyond the pylorus and down to the point of obstruction. Unless the operator is thoroughly experienced in the use of this tube and unless successful passage is attained promptly, the desired objective of deflating the obstructed intestine will not be achieved and further damage to the bowel will be occasioned by the delay.

If obstruction is early, parenteral replacement of depleted fluids and electrolytes will suffice. When strangulation may be present, one or more blood transfusions should be given before, during, and after operation to replace the plasma lost into the obstructed bowel and to counteract the tendency to shock. Penicillin in heavy dosage (50,000 units every two hours) is begun at once and is continued until convalescence is advanced.

**SURGICAL TREATMENT**—The best surgical procedure, in general, is that which involves the minimal amount of manipulation. Spinal anesthesia is usually preferred. The abdomen is entered through a new incision rather than the old one, since a lateral approach to the area most likely to be the site of the trouble offers better exposure than a direct approach. The first step is to locate the point of obstruction; this is best accomplished by identifying the terminal ileum at the ileocecal junction, which is always distal to the area of obstruction, and proceeding upward along the collapsed unobstructed lower ileum to the point of obstruction. It is inadvisable to try to find the block by pulling out loops of distended bowel; this method is more time consuming and more injurious. When obstruction is simple and viability of the affected bowel wall is unimpaired, release of the offending adhesion is all that is required. In certain cases (for example, following removal of a gangrenous appendix) broad dense adhesions may have developed without impairment of the blood supply of the bowel but may have become too firmly fixed to permit release of the constricted area. Under such circumstances, if the proximal bowel is in relatively good condition, an ileocolostomy in continuity may be per-

formed rapidly in order to short-circuit the obstructed but not devitalized area. This procedure is inapplicable if the obstructed bowel shows evidence of circulatory damage, but it is rapid and effective if employed before devitalization has occurred.

Blood-tinged or brownish watery fluid free in the peritoneal cavity usually indicates the presence of a strangulated loop, which will generally be found immediately above the obstructing adhesion. Intestine which has been obstructed even for a few hours is edematous and atonic and may tear simply by the weight of the contained fluid; manipulations therefore should be minimal and must be performed with the utmost gentleness.

If an area of incipient gangrene is noted, the affected loop is released from its adhesions, brought out of the wound, and covered with warm saline packs to determine whether circulation and normal function will return or whether strangulation has progressed too far for recovery to occur. In case of doubt, an interval of ten to fifteen minutes may be allowed to determine the viability of such a segment of bowel, provided the general condition of the patient will permit the delay. Administration of a high concentration of oxygen during this period will encourage the return of normal color and contractility in occasional cases. Injection<sup>24</sup> of a small amount of procaine (1 per cent solution) around the vessels in the base of the mesentery of the involved portion of bowel may encourage more rapid return of blood supply by temporarily blocking the regional vasoconstrictor fibers. If contractility and healthy circulation have not returned within a reasonable time or if the patient is in poor condition, the questionable loop should be removed. Resection with anastomosis of obstructed intestine is not always possible; the gangrenous loop must be removed, but operative repair upon damaged bowel may be dangerous. After adhesions have been released, the devitalized loop is brought out of the wound and excised between clamps. If the proximal bowel end is in reasonably good condition, anastomosis is performed; if the bowel is markedly distended, atonic, edematous, or congested, or if the patient is in poor general condition, primary anastomosis is unwise. In the latter case, a drainage tube is tied securely into each open end of the intestine as soon as the incision is closed. Continuity of the double-barreled loop may be restored by any method

desired, as soon as the patient is able to undergo the second operation.

If the patient is too ill to endure the strain of exploration and release of adhesions or if the adhesions are too dense to permit a short-circuiting anastomosis, a temporary enterostomy is done quickly as close above the point of obstruction as possible. The Witzel procedure is probably the most generally satisfactory, with the employment of a catheter (16 or 18 French) subsequently drawn through the omentum and fixed to the skin with a silk suture passing through the wall of the tube but not into its lumen. An enterostomy is a poor procedure at best; there is always danger of leakage around the tube, with peritonitis or wound infection as a possible consequence. It is often the only procedure possible, however, when the obstruction cannot be released and the viability of the proximal bowel is threatened. Enterostomy is never used when viability of the bowel is lost; devitalized bowel is always exteriorized and removed.

Following operation, care of the patient is conducted as before, with use of gastroduodenal or Miller-Abbott tube suction until the bowel has regained its normal tonus, transfusions to combat the toxic and operative shock, and properly planned use of intravenous fluids and vitamin therapy. Penicillin or sulfadiazine is given parenterally for prophylaxis and the usual measures are taken to prevent development of pulmonary atelectasis and venous thrombosis.

### Paralytic Intestinal Obstruction

Adynamic intestinal obstruction is probably the most difficult type of intestinal block to recognize and treat successfully. Like postoperative mechanical obstruction, the paralytic form may develop unobtrusively and without definite signs as a continuation of the *functional intestinal paresis* frequently noted for the first few days after a laparotomy. In this type of intestinal obstruction also the final pathologic developments depend upon the accumulation of large quantities of intestinal fluids and gas in the small bowel, although the primary cause of obstruction here is the relaxation of the intestinal musculature and the total disappearance of effective peristalsis throughout the small bowel rather than the establishment of a mechanical block at any one

point. The rapid collection of fluid and gas causes the formation of segmented and closed loops, which then develop vascular changes and strangulation as the result of increased intraluminal pressure and atonic relaxation. Systemic toxemia appears early and is proportional to the degree of mucosal damage in the strangulated loops.

Symptoms of paralytic obstruction are those of complete intestinal inactivity. Since adynamic ileus is often associated with spreading or generalized peritonitis, the symptoms of the primary disease tend to overshadow those of the intestinal inactivity. Colic is absent and, since the intestinal atony involves the entire small bowel, distention and vomiting develop relatively early in the course. In many cases the primary disease is given so much attention that the adynamic ileus is not recognized until far advanced and difficult to treat. Paralytic ileus begins as intractable intestinal distention due to atony and progresses rapidly, without responding to treatment at all. Vomiting soon becomes constant and profuse, taking the form of a steady trickle of fluid from the mouth or the collection of large quantities of foul material in the greatly distended stomach rather than the forceful emesis typical of mechanical obstruction. Temperature, pulse rate, and leucocyte count are high and rise rapidly and steadily, the rise paralleling the clinical course. Auscultation of the abdomen reveals absolute silence, with perhaps an occasional metallic splashing tinkle as the result of accidental movement of fluid and gas in the distended and atonic loops of bowel.

Differentiation of adynamic obstruction from mechanical obstruction is of considerable importance, since the latter form responds well to early operation, while the paralytic type is treated by nonoperative measures. Paralytic intestinal obstruction characteristically appears within three to four days following operation; if obstruction develops more than a week after operation, it is almost certain to be mechanical in type, particularly if colic is present. If the patient has generalized peritonitis, however, the obstruction may be of either type. Roentgenologic examination usually is of help in the differential diagnosis.

Treatment of paralytic intestinal obstruction is always nonoperative. When it is suspected that the patient may be in

danger of developing this complication, prophylactic measures must be instituted. Prolonged nausea and vomiting are best treated by gastric lavage, with the subsequent institution of gastroduodenal suction or decompression by means of the Miller-Abbott tube. In the earlier stages the atonic small intestine sometimes may be effectively stimulated by Prostigmin (1:4,000), 1 c.c. hypodermically every two hours for six doses; by morphine, 10 to 16 mg (gr. 1/6 to 1/4) every four hours for four doses unless the respiratory rate becomes depressed below 15 per minute; or by hypertonic salt solution administered slowly intravenously in a dose of 100 c.c. of 5 per cent solution. Enemas are useless, since they do not stimulate peristalsis in the small intestine, but the frequent insertion of a rectal tube may make the patient more comfortable by emptying the colon. Heat tents and turpentine stupes sometimes help; the use of pure oxygen may be of very definite value (p. 436). Operation is useless since the entire small bowel is affected; enterostomy is contraindicated, because only a single loop can be drained by this means. Probably the most valuable plan of treatment includes introduction of the Miller-Abbott tube with constant suction drainage, parenteral administration of fluids as needed to maintain water and electrolyte balance, infusion of protein hydrolysate solutions by vein, administration of blood and plasma transfusions and of vitamin concentrates, and use of chemotherapeutic and antibiotic drugs according to the indications of the individual case.

Paralytic obstruction, once it has developed, as a rule will not respond to direct therapy. Since it is usually secondary to some other pathologic process such as generalized peritonitis, successful treatment of the initiating disease will result in restoration of normal peristaltic function in the intestinal tract and disappearance of the adynamic block. In this type of case, however, secondary mechanical obstruction may develop later as the result of peritoneal adhesions, after the paralytic block has disappeared. This is not an uncommon complication of peritonitis and may appear within a few days after the subsidence of the infection, although in some cases several years may elapse before secondary mechanical obstruction develops.

Milder forms of adynamic intestinal obstruction, such as the generalized intestinal atony seen in association with renal colic or fractured pelvis, usually respond to the use of intestinal stimu-



lants, although the intestinal atony, even without specific treatment, tends to disappear concomitantly with the pathologic condition that was responsible for its appearance.

### Peritonitis

Inflammation of the peritoneal cavity can be divided generally into two main groups with respect to etiology: aseptic and infective. Peritonitis may appear in the surgical patient as the result of intraperitoneal hemorrhage or exudation or of perforation of a viscus and leakage of its contents. It may be localized, spreading, or diffuse in nature.

**ASEPTIC PERITONITIS.**—Aseptic peritonitis may develop as the result of injury to the delicate serosa by mechanical trauma during operation, with the resultant formation of a sterile serofibrinous exudate. Such a peritoneal reaction is of little consequence in itself and produces little constitutional reaction, although occasionally the sticky exudate causes the formation of adhesions which may later bring about mechanical intestinal obstruction. In other cases chemical irritation may initiate a local or diffuse aseptic peritonitis, such as occurs in conjunction with the postoperative leakage of uninfected bile, urine, gastric juice, or fresh blood into the abdominal cavity. Slow leakage of these substances into the abdomen tends to produce sufficient local reaction to prevent diffuse spread of the irritant, and the effects may remain local in nature.

**INFECTIVE OR BACTERIAL PERITONITIS**—Infective or bacterial peritonitis usually is secondary to disease somewhere in the gastrointestinal tract, with perforation of the wall. By far the commonest cause of postoperative peritonitis is the acutely inflamed and perforated appendix. The progress and final outcome of the infection, when proper treatment is instituted, depend largely upon the extent of spread and the degree of localization. If the lesion of the diseased viscus has developed and progressed slowly, limiting adhesions will have developed around the affected area. Consequently, when perforation occurs, the resulting peritoneal infection is limited in extent and an abscess forms without contamination of the general peritoneal cavity. Symptoms and signs in such a case are localized in nature and consist of pain, tenderness, rebound tenderness, and

muscular rigidity over the involved areas; often a mass can be felt. If the parietal peritoneum is entirely uninvolved, as in a pelvic or subphrenic abscess, there may be few localizing symptoms. The constitutional reaction is relatively mild; temperature, pulse, and leucocyte count are all moderately but not markedly elevated.

When localization is incomplete, spreading peritonitis may develop as the result of diffusion of the infecting organisms into adjacent uninvolved areas. Such an event may be diagnosed by the spreading of pain, tenderness, and muscle spasm beyond the area of original involvement and by the concomitant increased severity of the constitutional symptoms, with progressive elevation of temperature, pulse rate, and leucocyte count. Vomiting and intestinal colic in patients with localized or early spreading peritonitis are reflex in nature and are occasional and symptomatic occurrences rather than persistent and severe. The pain characteristic of this form of peritonitis, in fact, is not colicky but is more sharp, continuous, and aching in nature, since it depends *not* upon obstruction to peristalsis but upon inflammation of the parietal peritoneum.

Diagnosis of intra-abdominal inflammatory processes is often obscured by the fact that while inflammation of the parietal peritoneum produces well-defined and well-localized pain, irritation of the visceral peritoneum produces no discomfort at all. An infectious process therefore may develop to a relatively advanced stage without causing much abdominal discomfort if the parietal peritoneum is not involved.

Diffuse generalized peritonitis, the most highly fatal form, appears following the sudden perforation of a viscus before localizing adhesions have developed around the diseased area, with spillage of infected intestinal contents into the abdominal cavity. Postoperative generalized peritonitis may be sudden in onset and overwhelmingly rapid in progression or it may appear in a mild form and develop slowly but steadily during the first few days after operation. Although such an occurrence usually is secondary to acute appendicitis with perforation, the diffuse infection may appear as the result of leakage from a suture line or from the perforation of an area of bowel not recognized to be damaged at the time of operation or devitalized during the operation. Generalized peritonitis is marked by the presence of free and

unlocalized pus throughout the abdominal cavity. The clinical course is generally of short duration and terminates in death in a very high percentage of cases.

Generalized peritonitis usually is accompanied by severe and widespread abdominal pain because of the inflammation of the parietal peritoneum. Marked rigidity of the muscles of the abdominal wall appears as a protective mechanism, and extreme diffuse tenderness is present. The constitutional reaction is exceedingly severe. The patient's temperature rises rapidly and steadily, often reaching 105 or 106° F., and the pulse becomes rapid, running, and rather hard. Distention usually is slight at first and there may be little pain. Vomiting soon begins and, as paralytic obstruction develops, the regurgitation of intestinal fluids becomes more and more profuse and intestinal peristalsis soon stops entirely. The cause of death from diffuse infective peritonitis is a combination of the effects of toxic absorption from the purulent exudate and from the bowel contents and of the excessive and constant loss of gastrointestinal fluids and electrolytes by continued vomiting. The clinical course is sometimes a matter of hours rather than of days and the typical picture is only too well known to every surgeon.

The causative organisms most commonly found are the colon bacillus, staphylococcus, nonhemolytic streptococcus, and the Welch gas bacillus. Mixed infections are commoner than infections with a single organism and carry a much higher rate of mortality. The type of infection and the clinical course of generalized peritonitis differ considerably according to the portion of intestine from which leakage has occurred; peritoneal contamination by stomach contents causes the lowest mortality, and peritonitis as a result of perforation of the lower ileum carries the highest mortality rate.<sup>13</sup>

Infection of the peritoneal cavity is followed rapidly by the appearance of a thin fluid exudate, the type and quantity depending largely upon the responsible organism and upon the extent of contamination. The exudate soon becomes thicker and more purulent and the intestinal walls become edematous, reddened, and rough in appearance. Somewhat later, when the exudate assumes a serofibrinous or fibrinous character, adjacent loops of bowel become adherent throughout the infected area and, while the infection does become localized into many pockets

between the intestinal coils, the bowel walls become so edematous and inflamed that toxic absorption and paralytic obstruction quickly develop. If the infection is overcome by the peritoneal reaction without the development of adynamic intestinal obstruction, the fibrinous adhesions may bring about a mechanical block in some cases. In general, paralytic obstruction of the intestine is more likely to develop as a consequence of spread-

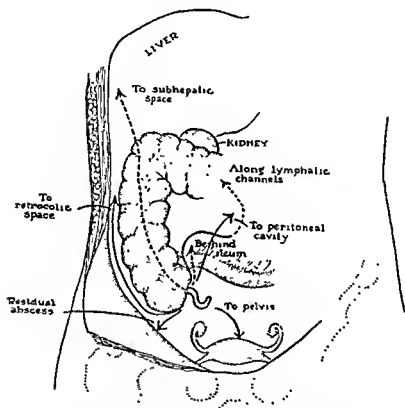


Fig. 44 —Possible routes of spread of infection from perforated appendix.

ing or diffuse peritonitis, while mechanical intestinal obstruction is most commonly found in association with localized intraperitoneal abscesses.

When the exudate is profuse, it tends to gravitate toward the most dependent areas of the abdominal cavity. From a pathologic process in the upper abdomen or along the right side, peritoneal fluid usually spreads to the right subphrenic spaces

or the lesser omental cavity, or along the right paracolic space or mesenteric root to the region of the cecum or down into the prerectal pouch (Fig. 44). Exudate arising from a lesion on the left side of the abdomen occasionally may reach the perisplenic area or lesser peritoneal sac but most often follows the left paracolic gutter to the sigmoid region and prerectal space. Well-localized pus in any of these areas can be drained without difficulty and without much danger to the patient, but pus which is pocketed between adherent loops of intestine cannot be reached surgically.

Treatment of peritonitis depends entirely upon the individual case and is often a matter requiring good judgment. Since there is no general agreement concerning proper methods of management, no fixed program of treatment can be devised. Certain broad principles of therapy are, however, widely accepted.

The aims of treatment include removal of the source of bacterial distribution, prevention of further spread of infection, restoration and maintenance of intestinal peristalsis, drainage and decompression of the atonic distended bowel, and preservation of proper fluid, electrolyte, and nutritional balance.

The probable location and nature of the responsible lesion should be determined, after which the general condition of the patient must be investigated carefully from every standpoint. If the patient can survive the procedure necessary to close the leak or to drain the source of infection, prompt operation certainly must be done. At the time of operation nothing should be done beyond the minimal necessary procedures. It is advisable to administer 1,000 to 1,500 c.c. of normal salt and dextrose (5 per cent) solutions in equal parts intravenously either before or during operation, particularly if vomiting has occurred or if acetonuria is present. Transfusion of blood or plasma also may produce improvement.

Emergency operative procedures in diffuse peritonitis are often attended by fatal results. Although it may be difficult to resist the temptation to perform an emergency operation promptly upon a patient who exhibits a true generalized peritonitis following appendical perforation, experience has shown that

the conservative treatment advocated as long ago as 1902 (A. J. Ochsner) is still a valuable procedure. Even though it is necessary to close a perforation in the appendix or cecum through which bowel contents are continuing to flow into the peritoneal cavity or at least to provide a drainage channel to the outside, preparatory measures must be instituted for a few hours to improve the patient's general condition. Operation, when performed, is designed not to treat the peritonitis itself but to attack the source.

Some confusion still exists concerning the indications for conservative therapy. This type of management was never advocated as a treatment for acute appendicitis but only as the safest method of handling patients who have developed generalized peritonitis with associated adynamic intestinal obstruction. Conservative treatment is directed toward the support and reinforcement of the natural defenses of the body against the spreading infection. Nothing is given by mouth and constant suction drainage of the gastrointestinal tract is instituted by means of the Wangenstein apparatus or, preferably, of the Miller-Abbott double-lumen tube. Suction drainage is, of course, a more recent addition to the original conservative regimen. Fowler's position has been advised, both to encourage accumulation of exudate in the pelvis rather than beneath the diaphragm or between loops of bowel and to permit unobstructed respirations. The value of Fowler's position in localizing exudate and decreasing absorption of toxic material in peritonitis has been questioned recently (p. 115); it is probable that the horizontal recumbent position is preferable unless the patient is more comfortable when propped up. The position is changed frequently to avoid development of venous thrombosis or of decubitus ulceration. Morphine, 10 to 16 mg. (gr. 1/6 to 1/4), may be given hypodermically several times during the day to insure the patient's comfort and to maintain tonus of the small bowel, but the use of opiates must be discontinued if the respiratory rate drops below 15 per minute.

Since the intestinal secretions are continually drained away by the suction apparatus and nothing is permitted by mouth, fluid replacement on an accurately planned basis must be carried out. The total amount removed by suction must be replaced

parenterally by an equal amount of fluid consisting of half normal salt solution and half dextrose (5 per cent) solution in addition to the basic quantity of fluid required to maintain normal fluid balance. Adequacy of fluid intake can be assumed if the daily urinary output averages from 1,000 to 1,500 c.c. and if the blood chloride level and carbon-dioxide combining power remain within the normal ranges. The administration of excess fluid, particularly of excess salt solution, will result in fluid retention; careful watch should be maintained for evidences of pulmonary edema, venous congestion, or peripheral edema.

While either penicillin or sulfadiazine alone in full dosage will effect a great decrease in average mortality from generalized peritonitis, the use of both drugs together is fully justified in such severe infections. Sodium sulfadiazine is slowly given intravenously in an initial dose of 5.0 Gm. in 100 c.c. of distilled water or by hypodermoclysis, in a similar dose, as a 0.5 per cent solution in normal salt solution. This is followed by a dose of 2.0 to 2.5 Gm. of the drug every eight hours as needed to maintain an effective concentration of 10 to 15 mg. of free sulfadiazine per 100 c.c. in the blood. Close watch is kept for early evidences of toxic reactions or of renal complications due to acetylsulfadiazine. Penicillin is administered intramuscularly in doses of 50,000 units every three hours throughout the day and night. Crile,<sup>16</sup> however, recommends much larger dosage and reports excellent results in treatment of appendical peritonitis by parenteral administration of penicillin in doses of 100,000 units every two hours for from four to six days, the dosage then being reduced to 100,000 units every four hours for six to eight more days. This author states that intra-abdominal inflammatory masses are absorbed spontaneously in most cases under this treatment without requiring surgical drainage. The unusually large dosage is advocated because such peritoneal infections are mixed in type; penicillin is active against gram-positive organisms but is inactivated in the usual relatively small dosage by the penicillinase produced by gram-negative intestinal bacteria.

If the peritoneal infection is known to be due largely or entirely to gram-negative bacilli or if response to penicillin and sulfadiazine therapy is inadequate, streptomycin is given intra-

muscularly in a dose<sup>17</sup> of 0.5 Gm. every four hours during the day and night. Adjustment of the dosage of all drugs employed is made in the usual way for children. Full doses are continued for several days after clinical evidences of infection have disappeared, after which the doses are reduced progressively over a period of two to four weeks before being discontinued entirely. Streptomycin, when used, is withdrawn several days after subsidence of symptoms; sulfadiazine and penicillin are continued for one or two weeks. It is probable that the combination of streptomycin with penicillin and sulfadiazine in full dosage will prove to be the most consistently successful form of drug therapy in bacterial peritonitis.

Frequent determinations of the nonprotein nitrogen and chlorides of the blood are made and the hemoglobin and hematocrit values watched closely. Hypoproteinemia develops promptly and progressively in patients with generalized peritonitis, and transfusions of blood and of plasma and infusions of protein hydrolysates or amino acid solutions all play an indispensable part in maintenance of normal nitrogen balance and nutrition. Vitamin concentrates, particularly of the B complex and C, are indicated in full therapeutic dosage. These measures are not to be restricted to the treatment of generalized peritonitis alone; the same principles of therapy apply equally to the routine supportive management of patients with localized or spreading peritonitis and should be followed with equal care in such cases until the danger of paralytic intestinal obstruction and generalized peritonitis is past.

Progress of the patient with peritonitis is followed with unremitting care. The return of peristalsis, audible upon auscultation, is one of the best indications of improvement and, conversely, persistent silence within the abdomen is of grave significance. The pathologic progression of paralytic intestinal obstruction to actual strangulation as a result of continued distention and fluid accumulation can be combated only by the maintenance of constant intestinal suction by the Wangensteen or the Miller-Abbott apparatus. As the patient's condition improves, the return of peristalsis may be detected by auscultation of the abdomen and confirmed by the introduction of a measured amount of fluid into the stomach, temporary discontinuance of suction



by clamping the drainage tube, and aspiration of the stomach contents at the end of a two-hour period. If the amount of fluid recovered is less than that introduced, it may be assumed that motor function is beginning to return to the bowel. While fluids may be given orally in small amounts during gastric suction drainage, the ingestion of large quantities of fluids should be discouraged. Electrolytes pass by transudation from the gastric mucosa into water retained in the stomach for even a short time; significant amounts of salt may be lost in this manner when the fluid is finally siphoned back from the stomach.

Drainage of the intestinal tract by means of an enterostomy is contraindicated in paralytic obstruction from any cause, since only one loop is drained thereby. Since the adynamic intestinal block is a direct effect of the generalized peritonitis, the intestinal atony will disappear concomitantly with improvement in the peritoneal infection. Mechanical obstruction may develop later in a patient recovering from diffuse peritonitis, as a result of fibrinous adhesions. Such adhesions usually tend to diminish and disappear with recovery from the infection and may not develop at all if intestinal decompression is maintained by means of a Miller-Abbott tube, which has its greatest usefulness in the treatment of cases of this type.

Other supportive measures are of considerable value. Small enemas are useful to reduce colonic distention as long as peristaltic function persists, and frequent insertion of the rectal tube may add to the patient's comfort. Local heat applied to the abdomen is often advocated to increase intestinal peristalsis and may be applied conveniently by means of a heat tent or by occasional turpentine stupes. Since diminution of peristalsis is of a protective nature, the use of powerful peristaltic stimulants is inadvisable; morphine, however, may be used to maintain intestinal tone but must be discontinued as soon as peristaltic function begins to return.

Oxygen is a valuable adjunct to treatment since the patient usually suffers from a moderate degree of anoxemia due to the abdominal distention, bacterial toxemia, and decreased respiratory amplitude. Orr<sup>18</sup> advocates the early institution of oxygen therapy and states that a nasal catheter placed into the oropharynx and delivering oxygen at a rate of flow of 6 liters per minute will produce an oxygen concentration of 50 to 60 per cent.

### Acute Gastric Dilatation

Acute dilatation of the stomach may appear after any type of operative procedure as well as in association with many varied nonsurgical conditions. Acute gastric dilatation is often noted in conjunction with the paralytic intestinal obstruction characteristic of generalized peritonitis, although it is relatively frequent also following operations upon the upper abdominal viscera. It is not an uncommon occurrence and is a possible complication in all early postoperative patients.

The characteristic clinical findings result from the rapid accumulation within the stomach of exceedingly large quantities of fluid and gas. The patient may have no complaints except a general sensation of vague abdominal pressure and discomfort, mild dyspnea, and marked weakness. Ordinarily, in conjunction with the rapidly progressive distention of the stomach shortly after operation, large quantities of watery, brownish-black fluid are vomited in a great gush, which is a significant and almost diagnostic occurrence. In an occasional case, however, there will be no vomiting, although a suggestive hiccup may be present. No alterations of temperature and respiration are consistently noted, although the respiratory excursions may be limited by the presence of the gastric distention. The pulse is always rapid and the rate continues to rise with the progress of the distention.

Examination of the abdomen reveals the presence of a slight fullness in the region of the stomach, which, in its distended state, may fill the entire abdomen and extend down into the pelvis. Respiratory movements may be limited on the left. The percussion note over the left side of the abdomen is flat, although a tympanitic note may be elicited high in the axilla. A well-defined splash occasionally can be produced by a gentle tap over the stomach area. Peristalsis is greatly decreased as a rule and nothing may be audible upon auscultation of the abdomen except an occasional tinkle. Diagnosis can be confirmed by the introduction of a stomach tube and aspiration of the total gastric contents, which often amount to several liters. In the ordinary postoperative case a Levin nasal catheter will suffice, since the contents of the stomach consist only of fluid and gas. Nonsurgical patients, however, who develop acute gastric

dilatation from some other cause may have solid food in the stomach which will block a small catheter and perhaps cloud the diagnosis; in such individuals a large stomach tube is more satisfactory.

**Pathogenesis.**—The pathogenesis of the condition is primarily on a reflex basis. As a result of excessive stimulation of either the visceral or somatic sensory nerves during an extensive operative procedure, the motor mechanism of the stomach, according to Dragstedt and co-workers,<sup>19</sup> may be inhibited powerfully by reflex impulses traveling along the vagus and splanchnic nerves, with consequent muscular atony. Acute gastric dilatation is particularly likely to occur as a result of such reflex inhibition in patients whose gastric motility has already been depressed by anesthesia or by chronic debilitating disease. The atonic stomach then may become rapidly distended by swallowed air and by duodenal fluid regurgitated through the pylorus. Such a condition can develop to a marked degree within the space of one or two hours and occasionally may occur even during the course of the operation.

The intragastric fluid is watery and is brownish or greenish-black in color, with a slightly bitter odor. It is almost neutral in reaction, contains little or no free hydrochloric acid, and is composed of gastric juice, bile, and the secretions from the pancreas and the duodenal mucosa. Since approximately 7 liters of digestive fluid are poured into the duodenum daily, it is not unusual to find several thousand cubic centimeters of fluid collected in the stomach within a few hours in a patient with acute gastric dilatation.

As the weight and size of the stomach increase, the distended viscus pushes downward into the pelvis, carrying the small bowel before it and producing a drag upon the root of the mesentery. As a result, the transverse portion of the duodenum, at the point at which it is crossed by the superior mesenteric artery, is occluded by the taut mesentery. The secretions of the upper digestive tract therefore continue to accumulate in the atonic stomach both as a result of the reflex inhibition of the gastric motor mechanism and as a consequence of the lower duodenal obstruction.

The direct systemic effects of acute gastric dilatation are due chiefly to the loss of body fluids and electrolytes by their

retention in the stomach. Dehydration, alkalosis, and occasionally even gastric tetany may develop as secondary complications and may present a puzzling picture until the dilated stomach is detected clinically. The condition is not often allowed to progress very far in patients who are suffering from peritonitis or paralytic intestinal obstruction from any other cause, since gastric retention is anticipated and proper therapeutic measures are instituted early. When such precipitating intra-abdominal disturbances are absent, however, acute dilatation of the stomach may not be recognized until the patient is actually moribund unless large quantities of fluid are vomited or unless the condition is identified by careful examination of the abdomen and introduction of a stomach tube.

Treatment consists in immediate removal of the contents of the distended stomach and relief of the drag of the mesentery upon the transverse portion of the duodenum. The accepted procedure formerly was to elevate the foot of the bed and keep the patient on his right side, but posture is no longer considered to be of major importance; the chief emphasis is now placed upon keeping the atonic stomach empty. Institution of gastroduodenal suction by means of the Wangenstein apparatus or of an acceptable modification is sufficient in most cases to relieve the distended stomach of its contents and to keep it empty until the return of normal peristalsis. Motor function usually reappears within forty-eight hours in the absence of peritoneal infection. By this means the secondary duodenal obstruction is relieved and the duodenal secretions are permitted to continue downward into the absorptive area of the ileum.

Drugs are not of much value in encouraging the return of gastric peristalsis. The depleted fluids must be restored by the intravenous administration of normal salt and dextrose (5 per cent) solutions, which are given slowly, in proper proportions and in sufficient quantities to insure a total daily urinary output of 1,000 to 1,500 cubic centimeters.

### References

1. Morgan, E. S., and Henderson, F. F.: Postoperative Intestinal Obstruction; Its Early Recognition and Management, *West. J. Surg.* 47: 471, 1939.

2. Lehman, E. P., and Boys, F.: *Clinical Use of Heparin in Peritoneum for Prevention of Adhesions, Report of 14 Cases*, Arch. Surg. 13: 935, 1941.
3. Wangensteen, O. H.: *Practical Aspects of Therapeutic Problem in Intestinal Obstruction, With Note Concerning Reaction Accompanying Conservative Decompression by Suction*, Internat. Clin. 3: 227, 1935.
4. Coller, F. A., and Maddock, W. G.: *A Study of Dehydration in Humans*, Ann. Surg. 102: 947, 1935.
5. Stone, H. B., and Owings, J. C.: *Acute Mechanical Intestinal Obstruction; Treatment and Results*, South. M. J. 30: 699, 1937.
6. Abbott, W. O.: *Indications for Use of Miller-Abbott Tube*, New England J. Med. 225: 641, 1941.
7. Whipple, A. O.: *Surgery of the Terminal Ileum, Cecum, and Right Colon*, Surgery 14: 321, 1943.
8. Smith, B. C.: *Experiences With Miller-Abbott Tube; Statistical Study of 1,000 Cases*, Ann. Surg. 122: 253, 1945.
9. Boehme, E. J.: *Management of Intestinal Distention (Adynamic Ileus), With Special Reference to Postoperative Distention*, S. Clin. North America 21: 560, 1944.
10. Gius, J. A., and Peterson, C. G.: *Postoperative Ileus and Related Gastrointestinal Complications, Critical Review*, Internat. Abstr. Surg. 79: 265, 1944; in Surg., Gynec. & Obst. Oct. 1944.
11. Hamrick, W. H.: *Technique for Introducing Miller-Abbott Tube*, U. S. Nav. M. Bull. 41: 1737, 1943.
12. Cantor, M. O.: *New Simplified Intestinal Decompression Tube*, Am. J. Surg. 72: 137, 1946.
13. Harris, F. I.: *Intestinal Intubation in Bowel Obstruction; Technique With New Single Lumen Mercury Weighted Tube*, Surg., Gynec. & Obst. 81: 671, 1945.
14. Fine, J., Hermanson, L., and Frehling, S.: *Further Clinical Experiences With 95 Per Cent Oxygen for Absorption of Air From Body Tissues*, Ann. Surg. 107: 1, 1938.
15. Harvey, H. D., and Meleney, F. L.: *Peritonitis; Collective Review of Significant Literature for Six and One-Half Years*, Internat. Abstr. Surg. 67: 339, 1938; in Surg., Gynec. & Obst. Oct. 1938.
16. Crile, G., Jr.: *Peritonitis of Appendiceal Origin Treated With Massive Doses of Penicillin; Report of 50 Cases*, Surg., Gynec. & Obst. 83: 150, 1946.
17. Pulaski, E. J., and Sprinz, H.: *Streptomycin in Surgical Infections. I. Laboratory Studies*, Ann. Surg. 125: 194, 1947.
18. Orr, T. G.: *Treatment of Peritonitis*, J. A. M. A. 113: 1489, 1939.
19. Dragstedt, L. R., Montgomery, M. L., Ellis, J. C., and Matthews, W. B.: *Pathogenesis of Acute Dilatation of the Stomach*, Surg., Gynec. & Obst. 52: 1075, 1931.
20. Herrlin, J. O., Jr., Glasser, S. F., and Lange, K.: *New Methods for Determining Viability of Bowel; Preliminary Report with Clinical Cases*, Arch. Surg. 45: 785, 1942.

## CHAPTER 15

### CARE OF THE WOUND

The progress of wound healing is influenced strongly by conditions existing before operation as well as by procedures performed in the operating room. Ideally, every clean surgical incision should heal rapidly and completely with minimum scarring, and every infected wound should respond promptly to treatment, permitting secondary closure or skin graft within a period of days rather than weeks. Optimum healing of this type requires proper observation of surgical principles and practical application of physiologic fundamentals.

Uncomplicated healing of a clean incised wound, either surgical or traumatic, takes place by primary or first intention. Following incision, the damaged cells on the cut surface exude tissue fluid containing substances which initiate sterile or aseptic inflammation. The apposed cut surfaces are glued together quickly by strands of fibrin and a thin layer of blood clot, and a little plasma seeps out on the surface to form a dry protective crust. The local blood vessels dilate, white blood cells migrate into the tissues, and the lymphatic flow increases. Dead and damaged cells are absorbed and carried away and contaminating bacteria are phagocytized. Within three or four days fibroblasts in the area of injury multiply and grow across the gap along the strands of fibrin, after which collagen fibrils are formed and the fibrin is absorbed. New capillaries bud from the small vessels in the region, and the injured area is quickly filled with loose spongy granulation tissue composed of new capillaries, fibroblasts, and collagen fibers. During this period, epithelium grows across the gap from each edge of the wound. As the connective tissue increases in amount, shrinkage occurs and the capillaries diminish in number, the fibroblasts regress, and the organizing scar increases rapidly in strength.

The healing incision is fairly strong during the first two days following operation when the sutures are at their maximum holding strength. During this period edema appears and, if the sutures are tied too tightly, some degree of anemic necrosis develops along the sutured margins. The wound consequently

is weakest from the third day until the sixth day, by which time fibroplasia and collagen deposition have provided some degree of firm union. By the tenth day growth of new tissue has reached its height and contraction of the scar has begun. Increase in wound strength therefore progresses rapidly from the sixth to the fourteenth day. Gain in strength is slow after this time but continues for some months.

Open wounds or wounds with loss of substance, in which the surfaces are not brought into apposition, must heal by a different process. The gap or defect is filled slowly by proliferation of granulation tissue from the bottom and sides of the area, a constant exudation of lymph and plasma occurring from the healing surface. As contraction of the newly formed fibrous tissue occurs in the deeper layers of the wound, the defect shrinks slowly and decreases in size. Eventually the entire wound is filled with a soft, red, spongy tissue which later contracts to form a dense firm avascular scar. Epithelial growth from the wound margins is prompt and complete across small defects; gaps larger in diameter than 2 cm. epithelize very slowly and become covered with a thin scar epithelium that has little resistance to trauma. Large open wounds will not epithelize; unless the entire defect can be closed by secondary suture, the granulating surface must be covered by a skin graft.

Granulation tissue is never sterile nor can it be sterilized; the moist surface covered with exudate affords a receptive medium for growth of most of the common contaminating bacteria. Infection rarely penetrates beneath the surface, however; the abundant blood supply effectively prevents the passage of microorganisms through even a thin layer of intact granulation tissue.

Bacteria are present as contaminants in any wound, even one made under surgically aseptic conditions. In most cases the number of organisms is so small that the tissue defenses prevent the development of clinical infection. When technique is poor and many bacteria are introduced or when conditions favoring bacterial growth are present, infection will develop in the incision and will require drainage. An area of necrosis and a gap in the tissues result, so that subsequent healing must occur by second intention rather than by primary union. Occurrence of a wound infection consequently delays convalescence by at least several days.

### Factors Influencing Wound Healing

Many of the conditions which interfere with normal wound healing are present before operation and may be detected and treated during this period. Other factors which delay normal repair take their origin in the operating room. Relatively few deterrents to primary healing develop initially during the post-operative period.

*Deficient oxygenation* of healing tissues retards cellular proliferation and decreases local resistance to bacterial infection. The effect of local anoxia is always the same, no matter what factor is responsible for the diminished oxygen tension. Anemia is one of the commonest causes; dehydration and overhydration also will interfere with oxygen transport. Systemic visceral disease reduces the circulatory efficiency in some cases; wounds do not heal well in patients with malignant neoplasms, in cardiac patients who exhibit congestive failure or diminished cardiac reserve, or in diabetic patients whose carbohydrate metabolism is seriously disturbed. Arteriosclerosis will reduce the blood supply to a healing area, and advanced age alone brings about many physiologic changes which impair the rate of healing. Other factors which tend to reduce oxygen supply to a healing wound include pulmonary disease or complications, postoperative decrease in vital capacity, the presence of any condition interfering with normal respiratory exchange, and failure to improve the vascular circulation by proper exercises while confined to bed.

Tissue anoxia is due frequently also to local causes. Heavy sutures placed too closely and tied too tightly defeat their purpose by strangulating the tissues. Some degree of local edema always develops following operation; the suture material used should be the lightest that can accomplish the desired result with perfect safety, and sutures should neither be placed too closely nor tied too strongly. Rough handling during operation, the use of heavy retractors, and the drying of unprotected wound surfaces cause local vascular damage as well as tissue injury. Even the application of a tourniquet may produce permanent destruction of an indispensable blood vessel, as in an older patient with arteriosclerosis. Tight dressings on an extremity have been known to cause distal gangrene, and the occurrence of pressure ulcers under a plaster cast is by no means uncommon. The type



of tissue itself also has some relation to rate of healing; areas of high vascularity such as the face and the stomach heal much more promptly than areas such as the pretibial region and the large bowel. The dependent position interferes with venous drainage; wounds on the extremities heal better if the extremity is elevated, at intervals if not constantly.

A constant and adequate supply of *other nutritional factors* in addition to oxygen is necessary for proper healing. Clinical application of an extensive amount of research has demonstrated that dietary proteins and vitamins have a direct and integral relationship to the rate and strength of wound healing. Raydin and associates<sup>1</sup> have emphasized the facts that an extra supply of protein is required for tissue repair and that hypoproteinemia delays healing and decreases scar strength. It is more than probable that protein deficiency is one of the chief factors in causation of wound dehiscence; certainly debilitated hypoproteinemic patients show a prompt and marked improvement in progress of healing and in rate of convalescence when an adequate supply of protein is provided.

The role of the *vitamins* in tissue repair is less definite; there is no conclusive evidence that any vitamin except vitamin C is directly concerned. It has been observed both clinically and experimentally in human subjects<sup>2</sup> as well as in laboratory animals<sup>3,4</sup> that prolonged depletion of ascorbic acid will delay wound healing, decrease the amount of collagen in the healing wounds, diminish the strength of repair, and even prevent union in the presence of other deterrents to healing. Deficiencies of other vitamins, such as those of the B complex, are likely to interfere with wound healing because of effects upon the general health and metabolism rather than upon the damaged tissues themselves.

Various *local factors* in addition<sup>5</sup> to those already mentioned may interfere with wound repair. Closure of an incision without proper anatomic approximation of tissue layers or with excessive tension upon the sutured structures, undue motion of the wound area, presence of a dead space, or development of a hematoma will cause separation of the wound surfaces and will prevent union. The presence of a nonabsorbable foreign body, whether necrotic tissue, suture material, drain, or extraneous substance, is often the explanation for failure of a wound to heal. External

fistulas connecting various viscera with the surface of the skin will remain open permanently if the mucosa of the internal organ lines the entire tract and joins with the external skin epithelium, even though the fistula performs no useful physiologic function. Infection, particularly with pyogenic organisms, is one of the commonest and most troublesome conditions interfering with normal wound repair. The occurrence of infection may not only threaten the life of the patient, but also may cause widespread local destruction with extensive and permanent scarring and impairment of function.

These untoward conditions may occur singly or in any combination; one or more of them will be present to some extent in every surgical case. The healing of an operative or traumatized area progresses at a rate largely determined by the extent to which such unfavorable influences are prevented or are treated as they develop.

### Technique of Changing Dressings

Sterile technique is indispensable in performance of wound dressings. The patient has every right to expect no less than the best care his attendants are capable of giving him; every precaution must be taken to avoid introduction of new contaminating bacteria into the wound. It is possible to get by with short cuts in technique in most cases, but the inevitable unwanted infection is bound to develop sooner or later, perhaps in the very patient in whom it will prove most dangerous. Observation of the rules of aseptic methods should be made routine; proper technique should be so reflex in nature that violation of it will be all but impossible. Careless handling of sterile materials, on the other hand, is a progressive habit. Poor technique usually grows steadily worse until trivial errors become major ones and postoperative infections may spread from an operating suite or through an entire surgical service. Bacteria do not "overlook" lapses in technique; they are always present, ready for introduction into a receptive area.

A surgeon or a surgical attendant should wash his hands before, as well as after, changing a dressing. Before the old dressing is removed, the availability of all the necessary sterile instruments and supplies is verified in order to avoid exposure

of the patient's wound while the required material is sought. If the dressing will be painful and prolonged, the patient should be given an appropriate dose of a narcotic drug. Gentleness, patience, and deliberateness are requisites in a surgeon who must perform painful manipulations on an unanesthetized patient; there is no substitute for sympathy and consideration under these circumstances.

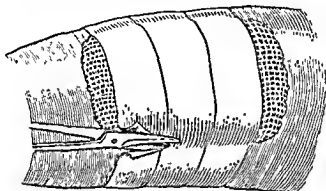


Fig. 45 — Removal of dressing. Fresh dressing can be fixed with new tape applied over the old tape.

Adhesive tape is removed slowly by stripping the skin away from the undersurface of the tape rather than by simply pulling off the adhesive. Sudden jerking of the tape, on the premise that quick removal gives pain for a shorter length of time, is never advisable; areas of skin may be torn off with the tape in individuals with delicate skin or with sensitivity to adhesive. Application of a sponge wet with ether or benzine between tape and skin will simplify removal. If tape is to be reapplied, the original strips need not be removed but may be cut at the edge of the dressing, the new strips later being applied over the old ones (Fig. 45). Painting the skin with compound tincture of benzoin, rubber cement, or a liquid adherent before application of tape will afford a sticky surface that encourages adhesion and decreases pain on removal.

The dressing is removed in the direction of the incision rather than across it (Fig. 46) to avoid traction on the wound edges with possible separation. A sterile towel is applied over the bedclothes below the wound and is tucked around and be-

neath the covers to prevent contamination if the patient should move suddenly. The nurse, using a sterile clamp, supplies the operator with sterile forceps and places several sterile sponges upon the towel (Fig. 47). The sponges are picked up in forceps and are used in succession to clean the wound area, a small amount of the requisite solution being poured upon the sponge over a basin. Neither the sponge nor the end of the clamp may be touched with the fingers or with the lip of the bottle, nor should a sponge be used more than once. A sterile applicator or spatula used to apply medication to a wound may be used only once and may never be reinserted into the stock bottle or jar of medication.

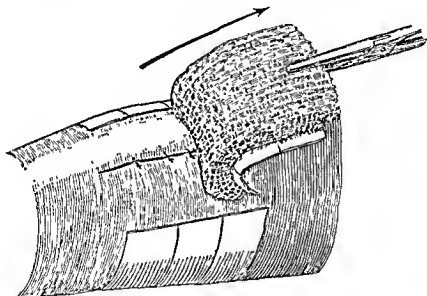


Fig 46.—Removal of dressing. Traction is made parallel to the incision rather than across, to avoid separation of wound edges.

The area of the wound is sponged concentrically from the center outward; once the sponge has covered the skin beyond the incision it may not be brought back again to the wound area (Fig. 48). As a rule, alcohol (70 per cent) is the preferred antiseptic for closed wounds; ether is just as satisfactory but patients often object to the odor and the cold sensation. Iodine is unnecessarily strong and may cause burns; other antiseptics stain

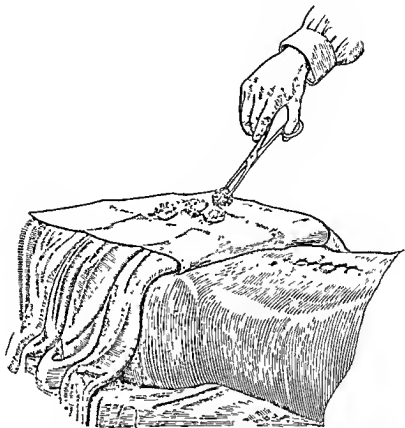


Fig. 47 —Change of dressing. A sterile towel serves as an instrument table

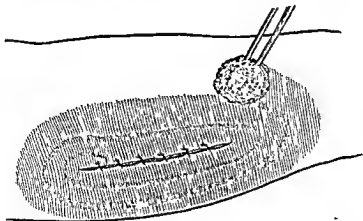


Fig. 48 —Change of dressing The wound area is sponged concentrically with antiseptic.

the tissues and obscure signs of inflammation. Care is taken to avoid introduction of antiseptic solution into open areas of the wound; exudate may be mopped or washed away safely with hydrogen peroxide or sterile normal salt solution with less pain and less damage to the tissues. Inspection and cleaning of the wound is followed by application of a light dry gauze dressing.

Every dressing tray or carriage is equipped with a large pair of dressing forceps kept in a container of alcohol. These forceps are used to remove sterile dressings or sterile instruments from their respective containers and are never used for any other purpose. If touched by any object that is not or may not be sterile, including the instruments used during performance of a dressing, the utility forceps must be discarded and not used again until after resterilization. Such a contaminated clamp may not be replaced in alcohol on the supposition that contaminating bacteria will be destroyed. Similarly, the fingers or an unsterile clamp never under any circumstances may be introduced into a sterile jar or stock container. Even though nothing is touched except the desired object, lint or threads or dust particles fall from the sleeve into the sterile container and may carry infection to the next patient. Moreover, the disinfectant solutions used to preserve sterility of the utility clamps cannot be depended upon to destroy spores or organisms buried in a smear of exudate or in a film of oil left as a fingerprint when the clamp has been contaminated by accident. It is scarcely possible to place too much emphasis upon the use of a well-informed habitual aseptic technique; such precautions when uniformly and honestly observed under all circumstances occupy little extra time and pay the greatest possible dividends in uncomplicated recovery of patients who require surgical operation or treatment of burns and open wounds.

**Sutures.**—The optimum time for removal of sutures varies with the location of the wound, the degree of tension, and the condition of the tissues. There is some variation according to individual preference but in general skin sutures are removed from the face in four to five days, from the neck in three to five days, from the anterior chest and abdominal wall in seven days, from the back and extremities in eight to nine days, and from the hand and foot in nine to ten days. The same times of removal apply when Michel clips are used for closure. Ordinarily the

first change of dressing after operation is done when the skin sutures are to be removed; it is done sooner, however, if evidences of wound complication appear or if the outer layers of gauze become stained by exudate.

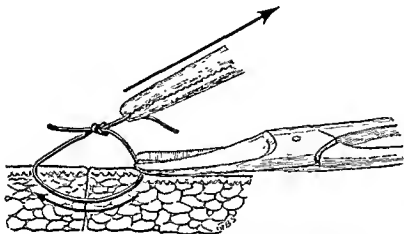


Fig 49 --Removal of sutures. Traction is made across the wound, to avoid separation of edges.

Stay or retention sutures which pass through the skin and deeper fascial layers remain for twelve to fourteen days; through-and-through retention sutures (for example, silver wire) are allowed to remain for fourteen to twenty days, especially if no other sutures were used in closure. If infection develops, enough sutures are removed to insure adequate drainage. When sutures, particularly stay sutures, are tied too tightly, evidence of necrosis as a result of strangulation may appear; removal of the most seriously offending suture will often afford enough relaxation to permit retention of the others. Sutures that are tied too tightly cut into the tissues and not only cause partial strangulation of the deeper tissues with more marked fibrosis, but also encourage infection and may produce permanent transverse scars in the skin. Sutures are removed by lifting the knot, clipping the strand at the level of the skin, and pulling the suture across the wound (Fig. 49); traction away from the wound may cause slight separation of the edges. Small superficial gaps in the skin incision can be closed by application of a narrow strip of adhesive

tape, freshly removed from the roll without touching the surface to be applied to the wound and passed several times through the flame of an alcohol lamp (Fig. 50). Sutures are allowed to remain a day or two longer than usual in a patient who is expected to show delayed healing (closure under tension, presence of malignant disease, arteriosclerosis, anemia, or malnutrition).

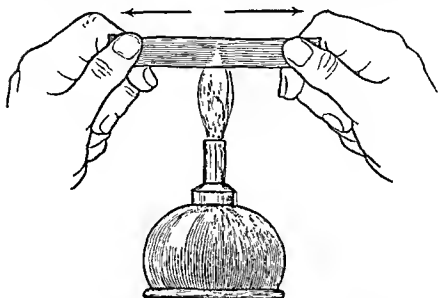


Fig. 50 —Adhesive tape, flamed in alcohol lamp, can be used for approximating unhealed wound edges

Pressure dressings are used in treatment of burns, traumatic lacerations, and large open wounds that can neither be sutured nor grafted immediately. Dressings of this type are applied or changed most safely in the operating room, where aseptic technique is observed, including the wearing of caps and masks and the use of sterile gloves.

If these dressings are changed on the wards, similar precautions should be followed. Open wounds are exposed and dressed only after the ward is quiet, visitors have departed, dust has settled, and tobacco smoke has cleared. Caps and masks are used, sterile gloves are worn, and care is taken to avoid both the introduction of new bacteria into the open wound and the transmission of bacteria from one patient to another. Contamination of such unprotected surfaces with small numbers of staphylococci and nonhemolytic streptococci is to be expected; these organisms



normally are found on the skin and will not usually cause a clinical infection. Addition of hemolytic cocci or proteus or pyocyanous organisms to the bacterial flora of an open wound, however, occurs secondarily during the course of treatment in most cases. While often unavoidable, infection due to these organisms is an unwelcome complication, since it is so difficult to eradicate and so likely to prevent successful secondary closure or skin graft. *Proteus vulgaris* and *Pseudomonas aeruginosa* are ubiquitous organisms; it is difficult to exclude them from open wounds which must be dressed repeatedly. Since the minimum damage that results from such infections is a prolongation of the patient's hospital stay by several days or weeks, the extra time and expense necessitated by aseptic technique in changing dressings is a small price to pay for the increased safeguards against contamination.

After the old dressing is removed, a piece of rubber sheeting is placed on the bed beneath the part to be dressed and is covered with a sterile towel. Another sterile towel is placed over the bedclothes nearby as a receptacle for sterile sponges and dressings. Fresh gauze is placed lightly upon the open wound and the surrounding skin area is cleaned of dried exudate and drainage by means of sponges soaked in hydrogen peroxide, normal salt solution, boric acid solution, alcohol, or ether. A basin is held beneath the wound to catch overflowing solution, and contamination of the bed is prevented by the rubber sheeting. When the skin is clean, the wound is inspected. As a rule, it is safer to avoid disturbing the wound surface at all, in order to minimize the danger of introducing fresh contamination. When obviously purulent exudate is present or when signs of infection and cellulitis are seen, a culture is taken and the wound is sponged lightly with normal salt or boric acid solution. Appropriate measures are instituted to treat the infection. If the wound is not clinically infected, immediate reparative surgery may be performed or a fresh pressure dressing may be applied.

A single layer of dry or impregnated fine-meshed gauze or closely woven cloth (p. 468) is placed upon the wound surface as smoothly as possible. A layer of several thicknesses of flat gauze sponges is applied next. This layer may be fixed lightly with strips of adhesive tape to prevent displacement if the dressing is on an area which is not splinted and is free to move. Upon

the flat gauze is placed a layer of fluffed gauze, or mechanics' waste, sufficient to make a dressing two to three inches thick when compressed. The dressings are held in place loosely by several turns of a gauze bandage or of a gauze roll, following which a woven cotton elastic bandage is applied snugly. A pressure dressing should extend five to six inches beyond the edge of the wound and should be applied snugly but not tightly. Plaster splints are not necessary for immobilization in the absence of fractures if the pressure dressing includes the joint above and the joint below the wound. In any case, when a pressure dressing is applied to an extremity, the entire length of the extremity distal to the wound must be included in the dressing to prevent distal edema and venous congestion.

Largely as a result of experience<sup>6,7</sup> gained during World War II, there have been radical changes in the treatment of traumatic wounds. Fresh wounds that are unsuitable for immediate closure are treated primarily by irrigation with sterile normal salt solution, careful thorough débridement, and application of a sterile pressure dressing. Antiseptic solutions are no longer applied to open wounds; even the use of sulfanilamide crystals locally is of questionable value (p. 480). Penicillin or sulfadiazine is given in appropriate dosage systemically for several days, blood transfusions are administered if indicated, and essential nutritional factors are supplied by a high protein, high vitamin diet. After four to six days the patient is taken to the operating room and the original pressure dressing is removed. In most cases, if preliminary treatment has been carried out properly, the wound will be clean and either secondary suture or split-skin grafting can be performed safely at this time. Bacteriologic studies are unnecessary; if the wound appears clean<sup>8</sup> and no clinical infection is present, definitive treatment can be performed. Postoperative care consists in application of a pressure dressing and continuance of chemotherapeutic and systemic corrective measures. Results of this method have been astonishingly good; scarring is minimal, functional recovery is maximal, and the patient spends only a relatively short time in the hospital. It should be noted that the use of chemotherapy, while certainly of value, is by no means the most important part of this plan of treatment. Success depends primarily upon the observation of fundamental surgical principles, including thor-

ough débridement, gentle handling of tissues, correction of nutritional deficiencies, and use of properly applied pressure dressings to insure local support, adequate immobilization, and avoidance of unnecessary dressings.

The progress of healing in open wounds is affected greatly by the dressings used. Ordinary gauze sponges are not satisfactory for immediate application to an open wound or to a burn; the openings between the gauze strands are so wide that granulation tissue either grows or is pressed between the threads and may cover them entirely. The dressing is difficult and painful to remove after several days have passed, and removal causes tearing of the granulating surface, with hemorrhage, edema, and increased susceptibility to infection. In like manner, the growth of new epithelium may be retarded or prevented by coarse-meshed gauze. Experience in the theatres of World War II has demonstrated that use of a fine-meshed material on open wounds encourages healing, reduces incidence of infection, and maintains a flat, healthy type of granulation tissue that is most satisfactory for reception of skin grafts. The best material generally available is fine-meshed gauze cut from sterile gauze bandages. The mesh of this gauze is wide enough to allow escape of secretions and yet fine enough to prevent adhesion to granulating wound surfaces. Appropriate lengths can be cut from bandage rolls of the proper width, put up in flat packages or containers, and sterilized. If cut gauze is not available, sterile instruments can be used to cut strips from a sterile bandage as the dressing is performed.

Gauze of this type is perhaps a little more satisfactory for application to open wounds if used dry than if impregnated with petrolatum, xeroform, or boric acid ointment. Addition of the grease causes blocking of the meshes, with interference to free drainage. Exudate retained beneath the dressing produces maceration of the wound edges, retards the formation of healthy granulation tissue and viable epithelium, and encourages the growth of bacteria. In addition to these disadvantages, gauze impregnated with ointment tends to stick together and form a solid wad or mass that may be more of a hindrance to healing than an aid.

The use of nylon surgical gauze (20 mesh) has been advocated by Bingham,<sup>\*</sup> who states that the mesh is fine enough

to prevent adherence to granulation tissue and that the material is sterilizable, chemically inert, and water resistant. It is probable, however, that nylon gauze of even finer mesh and lighter strands would be better, as he states. Soft linen, silk, rayon, and Fiberglas cloth have all been advocated as a dressing material for application directly to the wound; these materials are much more appropriate as dressings for burns than for wound surfaces, since the extremely fine mesh will allow serous exudate to pass but will become blocked by pus. Absorbent cotton, although soft and nonocclusive, is never suitable as a dressing for direct application to wound surfaces since strands are sure to become detached and remain buried in the healing tissues.

### Infected Wounds

The need for careful change of dressings is far greater in infected wounds than in clean ones; the infection must be kept restricted and not permitted to spread to other patients. The fingers may never be used to touch a dressing, especially one soaked with drainage or contaminated with pus. Rubber gloves should be worn or forceps used to remove even the tape holding a dressing upon an infected wound; unsterile bandage scissors used to remove the dressing must be sterilized before use on another patient's dressing. If the ungloved fingers accidentally touch a pus-soaked dressing, the operator should take time out immediately to wash his hands with green soap and rinse with alcohol before completing the dressing. Dirty gauze is deposited with care into a special bag that can be burned or a receptacle that can be disinfected at once. After completion of the dressing, the attendants who took part should wash their hands with soap and water and rinse with alcohol.

The aims to be accomplished in treatment of infected wounds, as outlined by Koch,<sup>10</sup> include (1) localization of the infection, (2) drainage following localization, (3) sterilization of the infected area, (4) covering of the raw surface or obliteration of the granulating cavity, and (5) restoration of function. For a full discussion of the local treatment of infected wounds, reference should be made to this article.

When frequent change of dressing is necessary, an improvised binder is used for fixation to avoid the irritation caused by repeated removal and reapplication of adhesive tape (Fig. 51).

Therapeutic aids to localization of a wound infection include (1) application of moist heat to increase local blood supply, (2) immobilization to reduce spread of the infection and to decrease discomfort, (3) elevation of the infected part when possible, to improve venous drainage and reduce swelling, and (4) chemotherapy, both to prevent general and local extension of the infection and to combat existing bacterial growth.

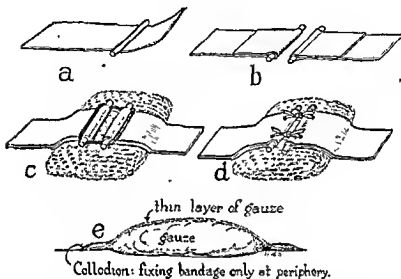


Fig 51 —Fixation of dressing. Montgomery binder permits frequent change of dressing without removal of adhesive tape. a, b, Broad strips of tape are partly folded back over fragments of wood (applicator sticks). The strips are fixed to the skin and are bound across the dressing either by rubber bands, c, or gauze ties, d. Note that the tape is doubled back sufficiently to prevent the adherent surface from touching the gauze dressing. e, A small dressing can be attached by placing a single layer of gauze over it and fixing the edges of the gauze with collodion.

**Wet Dressings.**—Moist heat applied to an infected area produces several beneficial effects. Local blood supply is increased by the heat, necrotizing and painful effects of tissue tension are reduced by the softening of the tissues, exudates are prevented from drying and obstructing further drainage, and necrotic sloughs are softened and loosened from the viable tissues. Wet dressings are used occasionally also as a vehicle for bactericidal agents.

While wet dressings are of much value in treatment of tissue infections, there are certain disadvantages associated with their use. Such dressings must be applied properly, maintained constantly at the proper temperature, and discontinued as soon as their purpose has been accomplished. Heat produces local hyperemia and raises tissue resistance; cold decreases local blood supply and reduces the resistance of tissues to infection. It is generally accepted that cold applications are contraindicated in local treatment of infections, yet a hot wet dressing improperly applied or allowed to cool becomes, in effect, a cold dressing. Also, prolonged soaking tends to cause edema and maceration of tissues; hot wet dressings should be discontinued as soon as the infection has localized, cellulitis and lymphangitis have disappeared, and necrotic tissue has softened. It is not an uncommon sight to see open lesions which are spongy, macerated, and edematous from too much soaking develop a prompt and healthy healing response as soon as the moist dressings or tubs are withdrawn. Finally, hot wet dressings are to be used with caution in treatment of infections in the presence of inadequate blood supply. Cellular metabolism, as well as local blood flow, is increased by heat; the tissue cells in a diabetic or an arteriosclerotic foot may be stimulated to activity beyond the capacity of the diminished blood supply to support. Hot wet dressings applied to an infected arteriosclerotic extremity are safe only if the progress of the infection is watched with the closest attention; otherwise tissue gangrene may appear and the infection may develop and spread far beyond its original potentialities.

There are many solutions suitable for use in wet dressings. Sterile normal salt solution is perhaps the best for all ordinary purposes; it is isotonic with the tissue fluids and is the least irritating solution available. Boric acid solution (2 to 4 per cent) is widely popular; it is nonirritating and exerts a slight antiseptic action. Magnesium sulfate solution in hypertonic concentration (10 to 30 per cent) has been suggested as a means of inducing active transudation of fluid outward from the wound, but this effect is apparently minimal and the macerating effect of the concentrated solution makes it unsatisfactory. Sulfanilamide solution (0.8 per cent) has been used to decrease surface bacterial growth but without notable success; it is subject also

to the disadvantage that tissue sensitivity to the drug may be induced. Other substances such as penicillin, streptomycin, tyrothricin, Azochloramid, and acetic acid may be employed in wet dressings for specific infections; these will be described later.

Moist dressings may be applied as tub soaks, irrigations, or hot compresses. Each method has its particular indications, depending upon the location and the type of infection.

During the acute stage of the infection, a voluminous sterile gauze dressing is applied and is changed every twenty-four hours. The dressing should extend well beyond the area of cellulitis in every direction; if the infection is located on the hand or foot, the dressing should extend to the axilla or inguinal region in order to prevent or combat tubular lymphangitis. A layer of gauze at least two inches thick is applied and is bound into place with a gauze roll, following which a sterile sheet of rubber or other waterproof material is placed around the entire dressing. The latter dressing is then covered with a bath towel or a sheet, pinned together to keep the dressings in place and to discourage motion. If the hot wet dressing is to be continuous, the outer covering and the waterproof layer are opened each hour or two and enough warm (110 to 130° F.) sterile solution applied to moisten the entire dressing (Fig. 52). The coverings are replaced and heat is supplied by hot-water bottles or, preferably, by a cradle containing one or more light bulbs. Solution is applied at whatever intervals are necessary to keep the dressings constantly moist; excess solution should not be used, nor should the bandages be allowed to dry. The dressings are changed aseptically each day and the progress of the infection noted; as a rule, compresses of this type, if properly applied, are not required for more than two or three days. If allowed to dry or become cold, these voluminous dressings may encourage progression of an infection; if carried on until the tissues are macerated, healing is delayed and local necrosis may be increased.

Areas of acute infection on the chest, abdomen, or back are treated similarly with hot wet dressings. After localization, the infection is drained by incision through a sterilized area of skin at which the infection is most superficial. Establishment of drainage usually is followed by prompt healing; if inflammation continues, hot wet dressings are again instituted for a day or two and the cause of persisting infection is investigated.

At times, maceration of the skin will develop before the infection has localized, and continuous compresses must be discontinued. Under these circumstances, the dressings are soaked in warm sterile solution for thirty minutes and then dried under a cradle and light (heat tent) or with an infrared lamp, the inter-

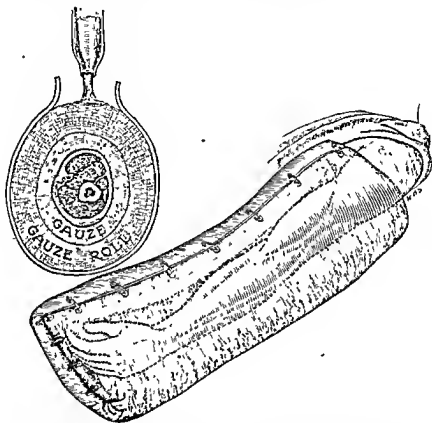


Fig. 52 — Hot wet dressing. The skin is coated lightly with sterile petrolatum. Fluffed gauze sponges are applied and held loosely in place with a gauze roll, and the arm is wrapped in a cellophane or rubber sheet, which is opened at intervals to allow moistening. The dressing covers the entire extremity. Heat is supplied by hot-water bottles or heat tent.

mittent soaking being repeated several times a day. It is not advisable to allow any wet dressing to dry at room temperature; it then becomes, in effect, a cold dressing. Treatment of this type is especially advantageous in the care of subsiding infections in the hand or foot. It is not necessary to remove or



change the dressing more often than once daily as long as the skin is unbroken and there is no drainage of exudate.

The practice of wringing out small compresses and applying them at intervals to an infected area is not effective enough to justify the effort. Unless the attendant is unusually gentle, the inflamed area is traumatized slightly each time the dressing is changed and the dressing usually is more cold than hot. It is preferable, especially in conditions such as infections of the face, to allow the dressing to remain in place and to moisten it at intervals by means of a medicine dropper; such a dressing should not be saturated. Continuous heat can be supplied by a lamp. Whenever compresses or wet dressings of any type are to be used, a light coating of petroleum jelly should be applied to the skin to decrease the macerating effect of the soaking.

Continuous irrigation by the Carrel-Dakin technique is no longer widely used in this country. Although this treatment was of the greatest possible value in the past, more recent methods in management of large infected wounds will produce equally good results with expenditure of much less effort. Proper use of Carrel-Dakin irrigation requires close attention to detail, unvarying promptness in introduction of the solution, and considerable familiarity with the technique. If the treatment is not carried out properly, it is of little or no use and may even produce irritation of the tissues. Dakin's solution has not been included in the latest United States Pharmacopeia.

### Local Medication

The effect of drugs used for local application to the unhealed wound surface is limited; there is little absorption either through the intact skin or through granulation tissue. Certain specific purposes can be accomplished by local medication, however.

Bactericidal and bacteriostatic agents can effect a reduction in the number of microorganisms present in an open wound but cannot sterilize the wound surface. Superficially placed bacteria are destroyed by application of an antiseptic, but bacteria located deeply in the crevices of the wound and buried in the film of surface exudate are not reached by the drug and continue to grow. As a rule, strong antiseptics do more harm than good when applied to an open wound; most bactericidal

agents are also protein precipitants and cause a coagulative necrosis of the surface layer of tissue cells. The resulting exudate and necrotic surface film furnish an excellent medium for growth of the remaining viable bacteria. Clinical infection therefore is even more likely to develop following use of an antiseptic than if the antiseptic is omitted. Most people who habitually apply iodine or alcohol to small accidental lacerations expect the wounds to become reddened and painful during the next few days, although simple irrigation of the fresh wound with tap water and application of a small unmedicated sterile bandage is much more likely to be followed by rapid and painless healing. Even large traumatic wounds are treated best by simple irrigation with sterile normal salt solution under aseptic precautions, thorough débridement, flushing with more salt solution, and application of a pressure dressing.

The same principle is equally true of surgical wounds. The use of strong antiseptics on exposed tissue, whether infected or uninfected, will produce further delay in healing and increase in severity of infection rather than improvement.

*Irrigation* of infected wounds effects mechanical removal of exudates and surface bacteria, promotes free drainage, softens dried crusts, encourages separation of sloughing and necrotic tissue, and removes irritating substances from the wound and skin surfaces. Bacterial growth is inhibited and healing is aided by periodic cleansing of a draining wound. The chief danger of the procedure is that new strains of contaminating bacteria may be introduced during the treatment, with mixed infection resulting. This can be minimized by observance of proper technique.

Irrigations can be performed by means of a sterile infusion set with a blunt glass nozzle or more simply with a bulb syringe and a sterile cup or glass. The bed is protected with a rubber sheet and the solution is allowed to drain from the wound into a basin. Particular precautions to be observed include the use of masks by the attendants to avoid introduction of hemolytic staphylococci or streptococci into the wound, the use of rubber gloves to avoid addition of proteus or pyocyaneus organisms to the flora already present, and the exercise of care to prevent spread of infection to other patients. Sterile normal salt solution is the most generally acceptable solution for wound irrigation; boric acid (2 to 4 per cent) also may be used. If the wound

is large, the solution should be warmed to 90 to 100° F.; cold solutions may be uncomfortable to the patient. Hydrogen peroxide is useful to loosen dried exudate and thick pus, but the tendency of peroxide to dissolve fresh blood clots and induce bleeding must be remembered. The wound is given a final flushing with normal salt solution and a pressure dressing is applied until time for the next irrigation.

Daily change of dressing in such cases is combined with proper systemic therapy such as high protein diet, blood transfusion, use of vitamin concentrates, and systemic chemotherapy until the granulating wound surface is clean and healthy in appearance, no evidence of cellulitis or infection is visible, and the exudate is scanty, thin, serous, and odorless. Secondary suture or split-skin grafting then may be performed with reasonable certainty of success. An infected wound which is being prepared in this manner for repair must be dressed and irrigated regularly each day for as long a period as necessary and, above all, on the day before definitive treatment is attempted. Drainage-soaked dressings pressed tightly against a wound surface cause maceration and edema; failure to change the dressing on even a single occasion may result in regression of improvement, growth of newly added contaminants previously held in check by daily dressing, and postponement of operative repair. Operation should not be attempted unless the dressing was changed the preceding day. Since each postponement of repair adds to the patient's hospital stay, increases the debilitating drain on the bodily resources, adds to the formation of scar tissue, and promotes further impairment of function, the omission of a scheduled dressing may produce untoward results out of all proportion to the time and trouble involved. Obviously, this plan of treatment applies only to infected or dirty wounds; clean traumatic or operative wounds should be repaired at the time of the first change of dressing if their appearance is clinically satisfactory (p. 467).

*Soap* is used widely for the cleansing of skin as well as of traumatic wounds. The chief effect of scrubbing the skin with soap is to remove the surface film of grease and oil normally present on the skin and the transient contaminating bacteria which have been picked up by contact with various objects. Cultures taken from the skin following a ten-minute scrub are

not sterile but show growth of the less virulent organisms normally inhabiting the depths of the skin glands and the crevices about the fingernails. Cultures taken from the unscrubbed skin may show bacteria of almost any type, commonly including hemolytic staphylococci, hemolytic streptococci, gram-negative intestinal bacteria, *Proteus vulgaris*, and *Pseudomonas aeruginosa*. The coccal organisms find their natural habitat in the mouth, nose, and throat, especially during the winter season; the bacteria are normal inhabitants of the bowel and may remain viable on the fingers for hours if the hands are not properly washed after contamination. The transient flora of the skin can be removed more effectively by proper scrubbing than by the use of antiseptics; the permanent flora remain in spite of both scrubbing and disinfection. Contamination of a wound with the latter organisms, chiefly nonhemolytic staphylococci and streptococci, is not likely to produce a serious infection unless predisposing factors are present.

The use of white soap and even of tincture of green soap is advocated by many authorities for cleaning fresh traumatic wound surfaces. By this method, a dry sterile sponge is inserted lightly into the wound, the surrounding skin is scrubbed thoroughly with soap and sterile water for from five to ten minutes and the soap is flushed away with sterile water. The gauze is removed from the wound and the laceration is sponged gently with white soap and sterile water on cotton balls, an effort being made to reach all crevices of the wound and to remove all surface exudate and dirt. The soap is removed by irrigation with sterile normal salt solution and débridement is performed. However, while soap does not destroy tissue cells, it has an irritating effect; furthermore, it cannot reach bacteria buried in the recesses of the wound. It is possible also that rubbing and massaging of the tissues during washing may lodge deeply placed bacteria still more firmly in the tissues. For these reasons, although soap is unsurpassed as a cleaning agent for the unbroken skin, simple irrigation of a wound with sterile normal salt solution is preferable to washing with soap as a preliminary to débridement. If soap is used at all in the wound, white soap is preferable to tincture of green soap.

*Alcohol* is an excellent antiseptic; it is usually employed in 70 per cent concentration for disinfection of the skin. Because it is a powerful protein precipitant, alcohol should never be intro-

duced into an open wound or applied to a mucous surface under any circumstances. Accidental spilling of strong alcohol into deeper sinuses or fistulous tracts is especially to be avoided; these channels cannot be sterilized and damage to the deeper tissues or connecting viscera may result.

*Ether* is a dependable antiseptic and a good fat solvent; it is somewhat irritating to the tissues but does not cause tissue necrosis. Because of these properties, ether may be used locally in wounds without harm. Its value as a wound antiseptic is limited, however, by its rapid evaporation and by its immiscibility with water or serum. The chief value of ether as a local application is in the removal of grease and oil from the skin before use of an antiseptic of more prolonged action.

*Iodine* (U. S. P. tincture, 2 per cent) exerts a powerful bactericidal action; it is one of the best antiseptics available. It cannot be used in an open wound; iodine causes prompt coagulative necrosis of tissue cells. When used for disinfection of the skin, iodine is applied lightly, allowed to dry thoroughly, and is removed completely by two or three successive applications of alcohol (70 per cent). Patients with delicate skin may suffer burns from iodine; it must be removed promptly and completely in all cases. If it is used for skin preparation in the operating room, puddles of iodine in alcohol should not be permitted to accumulate beneath the patient on the operating table. Iodine applied to an area previously coated with a mercurial antiseptic is very likely to cause a burn due to formation of the caustic mercuric iodide; the two types of antiseptic must never be used together. Adhesive tape applied to an area of skin cleaned with iodine may cause blistering and irritation. When used properly, however, iodine is one of the most effective and dependable antiseptics available; it is employed in many hospitals in routine preparation of the skin for operation.

*Merthiolate* and *Metaphen*, mercurial antiseptics, are available either as tinctures or aqueous solutions. They are non-irritating to the skin, and the tinctures (1:1,000) are satisfactory for preoperative preparation. Weaker aqueous solutions (1:10,000) are safe to use on mucous surfaces such as the conjunctiva and the urinary bladder. Mercurial antiseptics are protein precipitants and are not used in open wounds. *Mercurochrome* (2 per cent) is less used than in former years; its bacteri-

cidal action is less than that of the newer mercurial antiseptics and it stains the tissues more deeply. *Zephiran*, a proprietary antiseptic supplied in aqueous solution, is reported to be effective, inexpensive, and nonirritating but also should not be used on fresh wound surfaces.<sup>11</sup>

*Hydrogen peroxide* exerts its characteristic effect by liberating oxygen upon contact with the tissues, with tissue exudate, or with blood or serum. The slight bactericidal effect of the free oxygen is only incidental; the chief value of hydrogen peroxide lies in its detergent action. Crusts of dried exudate are softened and floated away, collections of pus and serum are emptied and cleaned, and the coagulated film present on every wound surface is dissolved and washed off, leaving the granulating surface clean and open. Hydrogen peroxide has two chief disadvantages; occasionally it may carry bacteria deeper into the tissues and it may dissolve fresh blood clots with some resultant bleeding. It is the best means available for loosening dressings that are stuck to the wound or to the skin by dried exudate.

*Sulfonamide* drugs applied locally are of little or no value in the treatment or prevention of wound infection. When sulfanilamide came into general use, its prompt effectiveness against the beta hemolytic streptococcus both in vitro and in invasive clinical infections led to the belief that it would be equally effective when used locally in fresh wounds. Over a period of several years, many clinical reports on this subject appeared, some stating that sulfonamides applied locally were of great value particularly in prevention of wound infection and others stating that they were of no value whatever when used in this manner.

As experience accumulated, certain technical considerations were found to be of importance. Sulfanilamide exerts its greatest effect against the beta hemolytic streptococcus; other organisms are less susceptible, or perhaps not susceptible at all. Sulfanilamide is very soluble; it is readily absorbed from a fresh wound surface and produces a high concentration locally in the tissue fluids for a few hours. In a very short time, the drug is carried from the wound area into the general circulation, and the bacteria remaining in the wound, relieved of the restraining influence of the drug, begin to proliferate. When used in large quantities locally, sulfanilamide may cause tissue irritation and also may interfere

with healing by acting as an unabsorbed foreign body. If applied indiscriminately to large wounds or burns, sulfanilamide may be absorbed rapidly enough to produce exceedingly high levels of the drug in the blood, with toxic effects; sensitization also may develop.

Sulfathiazole, somewhat more effective than sulfanilamide against staphylococci, has proved equally disappointing when used locally<sup>12</sup> in wounds. Sulfathiazole is of low solubility; even when used in microcrystalline form, it tends to remain in the tissues, unabsorbed for days. Either drug must be applied, if used, as a very thin frosting on the wound surfaces—sulfanilamide because it is absorbed so rapidly that a high systemic concentration may appear and sulfathiazole because it is absorbed so slowly that it may act as a foreign body and delay healing.

No sulfonamide drug applied to a wound can free the wound even of bacteria susceptible to its effect; microorganisms remain in wound crevices and tissue spaces to which the drug cannot penetrate. Furthermore, sulfonamides are bacteriostatic rather than bactericidal, final destruction of the organisms being accomplished by the leucocytes. Bacteria growing on fragments of necrotic tissue and on the surface of foreign bodies therefore may be hindered temporarily from multiplying and spreading into the living tissues of the wound, but they are not destroyed and are able to produce a wound infection as soon as the local concentration of sulfonamide decreases. In addition, other proteolytic bacteria present may be entirely unaffected by the drug and may themselves cause clinical inflammation.

Studies have been made on the effectiveness of local chemotherapy in prevention of wound infection by comparison of results in a large group of patients in whom sulfonamides were used with a similar group of patients in whom sulfonamides were not used, other details of treatment being the same. Meleney and Whipple<sup>13</sup> analyzed the results obtained in 2,191 patients, including those with soft tissue wounds, compound fractures, and burns, treated and observed at nine large medical centers throughout the country. The results showed consistently that sulfonamides applied locally to wounds have no effect whatever in reduction of incidence of infection but that sulfonamides administered systemically will reduce the incidence and the severity of infection spreading from the wound. Meleney and Whipple draw

the conclusion that "all the results seem to indicate that the main dependence of the surgeon on the prevention of infection both in civilian accidental wounds and in the war wounds must be placed upon the well known principles of the surgical care of contaminated wounds: namely, the removal of the devitalized tissue and the contamination, and the rapid restoration of the normal physiology of the part involved. The use of sulfonamides can in no measure make up for this."

Lyons,<sup>14</sup> investigating the value of chemotherapy in war wounds, came to the same conclusion: that chemotherapy is able only to counteract or minimize bacterial invasion, since sulfonamides can neither sterilize the wound nor stop decomposition of tissue. Local use of chemotherapeutic agents in tissue wounds consequently is of little or no value, while systemic administration of sulfonamides or penicillin is highly effective in the control of infection developing in and spreading from the wound. This author describes<sup>8</sup> the method evolved in World War II for repair of traumatic wounds (p. 467) and contrasts it to methods formerly in use. Reduced to simplest fundamentals, the Carrel-Dakin technique developed in World War I effected chemical digestion of dead tissue protein, the closed plaster method suggested by Orr and advocated by Trueta promoted bacterial digestion of necrotic tissue, while the current method of primary débridement, systemic chemotherapy, and early secondary closure accomplishes surgical excision of dead tissue.

*Penicillin*, although highly effective against gram-positive cocci, is not always effective alone in local application to wounds, either for prophylaxis or treatment of infection. Penicillin is freely soluble in water and is absorbed or lost from the wound in a very short time; clinical investigations are at present being made to develop a vehicle which will hold the drug on the wound surface for adequate lengths of time. A second and no less important disadvantage to the local use of penicillin in wounds is that many bacteria, particularly the gram-negative intestinal bacteria, produce an enzyme (penicillinase) which neutralizes the activity of the drug. Such organisms are common in mixed infections and will grow even more actively if the gram-positive cocci are destroyed. Penicillin is most effective in acute surgical infections due to the staphylococcus<sup>15</sup> alone.



When penicillin is used locally in aqueous solution, it is applied to the wound every hour or two by means of wet dressings. Sterile normal salt solution or distilled water can be used as a vehicle, the solution containing usually 1,000 units of penicillin per cubic centimeter. Individuals with wound infections severe enough to warrant local application of penicillin should be treated also by systemic administration of the drug in the usual dosage.

*Streptomycin* may be used alone for treatment of wounds infected with gram-negative bacteria, but its effectiveness is decreased greatly if gram-positive organisms also are present or if the fluid environment of the wound is acid in reaction. For local use, streptomycin is dissolved in sterile water or normal salt solution in amounts of 25 to 50 mg. per 100 c.c. and, if possible, buffered to pH 7.5 to 8.5. The solution is applied upon constant wet dressings which are changed several times daily both to allow free access of fresh streptomycin to the wound and to remove accumulated exudate. The effectiveness of the treatment is decreased by the necessity for frequent dressings, during which fresh contaminating bacteria may be introduced. A definite effort is made to control the infection quickly, within the first two days of treatment if possible, since susceptible bacteria may develop resistance or "fastness" to streptomycin with great rapidity.

*Other antibacterial agents* for treatment of mixed infections in wounds are being investigated clinically and experimentally. Penicillin occasionally may be fairly effective in the local treatment of infections due to gram-positive cocci alone, but it is of little or no value if gram-negative bacteria also are present. Streptomycin is highly effective against most of the common gram-negative bacilli but its activity is greatly reduced if the reaction of the medium or exudate is unfavorable (acid). Furthermore, if the concentration of either of these antibiotic agents is permitted to drop below the optimum effective level, bacteria ordinarily susceptible to their activity will rapidly develop resistance and become "fast." Before either antibiotic drug is used to treat an infection locally, therefore, it is advisable to identify the organisms causing the infection and to eliminate the ones resistant to the drug so that the therapeutic effect upon the susceptible organisms will not be reduced.

For these reasons, search is being made for substances to use in combination with penicillin or with streptomycin to eliminate organisms which interfere with their activity in treatment of mixed infections of superficial lesions. Meleney and associates,<sup>16</sup> after testing a large number of antibacterial agents, concluded that *parachlorophenol* appears to be of definite value for this purpose. Parachlorophenol was found to be highly effective against gram-negative bacteria, including *Escherichia coli*, *Proteus vulgaris*, and *Pseudomonas aeruginosa*, even in the presence of pus and necrotic tissue. By eliminating these bacteria in mixed infections, parachlorophenol eliminates their inhibiting effect upon penicillin applied simultaneously to combat the gram-positive cocci. Parachlorophenol is sufficiently soluble in water, is compatible with penicillin, and is nontoxic. The use of 0.25 per cent parachlorophenol in carbowax 4,000 - propylene glycol ointment, containing penicillin 1,000 units per gram, has been suggested for clinical use in treatment of infected wound surfaces. Directions for preparing the ointment are given in the reference cited.

*Nitrofurazone* (5-nitro-2 furaldehyde semicarbazone)<sup>16</sup> is similar in clinical use and effectiveness to parachlorophenol. When applied topically to infected wounds, it is bacteriostatic and bactericidal for most gram-positive and gram-negative organisms, although not consistently effective against *Proteus vulgaris* and *Pseudomonas aeruginosa*. It is available commercially (Furacin) in a water-soluble ointment base.

Howes<sup>11</sup> reports that a solution of Sulfamylon (5 per cent) and streptomycin (200 units per cubic centimeter) in sterile distilled water is nontoxic, stable, and clinically effective, with a wide range of antibacterial activity.

*Tyrothricin* is a mixture of two antibiotic substances produced by the spore-bearing soil bacillus, *Bacillus brevis*. One of the substances, gramicidin, is present in effective amounts and is bacteriostatic and bactericidal against gram-positive cocci; the other substance, tyrocidin, is not clinically effective but increases the solubility and stability of gramicidin.

This antibiotic is available in alcoholic solution, which for clinical use may be diluted with sterile water to make a solution containing 0.33 to 0.50 mg. of the drug per cubic centimeter. The solution can be kept in a refrigerator for several days without

deterioration Tyrothricin is suitable for local application only; it is too toxic for parenteral use and is of no value in treatment of systemic infections Tyrothricin produces hemolysis when absorbed and therefore cannot be used in local treatment of intrapleural or intraperitoneal infections.<sup>17</sup> It is ineffective when given by mouth. Howes<sup>11</sup> states that tyrothricin is too toxic to use upon any wounds except those with granulating surfaces.

The chief value of tyrothricin is in the treatment of superficial indolent infected wounds or ulcers, such as varicose ulcers of the extremities or shallow osteomyelitis cavities, in which the infection is due to gram-positive cocci. Organisms most susceptible to tyrothricin include *Streptococcus hemolyticus*, *Staphylococcus aureus*, and *Staphylococcus albus*.

Tyrothricin solution is applied locally as constant wet dressings or, much less effectively, by frequently repeated irrigations. Proper aseptic technique must be observed to avoid contaminating the wound with organisms refractory to tyrothricin. Following disappearance of gram-positive cocci from the infected wound, there may be rapid proliferation of gram-negative bacteria such as *Proteus vulgaris* and *Pseudomonas aeruginosa* (*Bacillus pyocyaneus*) if present. These bacteria, when freed from the growth-restraining influence of other proliferating organisms, tend to increase in numbers rapidly and to require specific therapy for control. Tyrothricin therefore is unsuitable for use in mixed infections. The bacteria responsible for a chronic wound infection should be identified before treatment is begun, tyrothricin gives best results in treatment of granulating wounds infected only with gram-positive cocci.

*Bacitracin*, discovered and under investigation by Meleney and Johnson,<sup>18</sup> is an antibiotic substance which is reported to be of considerable value for direct treatment of localized tissue infections caused by aerobic and anaerobic cocci. The range of therapeutic activity of bacitracin appears to be wider than that of penicillin, although some organisms susceptible to one drug are resistant to the other. Meleney states that when used locally the substance is not toxic or irritating and that it is not inhibited by the presence of blood, pus, necrotic tissue, or penicillinase-producing organisms.

During clinical study, the substance has been used both in aqueous solution (100 "units" per cubic centimeter) and in a

water-soluble base. For treatment of acute subcutaneous infections such as furuncles, abscesses, cellulitis, and felons, the aqueous solution is injected directly into the center of the lesion through a sharp needle, amounts of 0.1 to 5 c.c. being used according to the size of the infected area. Open lesions such as ulcers, chronic osteomyelitis cavities, and impetigo are treated by application of bacitracin ointment, often only a single treatment being required. The antibiotic has been used locally only.

Although bacitracin is neither generally available nor adequately investigated as yet, mention has been made of this drug because it appears to offer considerable promise as an effective antibiotic.

*Azochloramid (chloroazodin)* releases small amounts of free chlorine at a constant rate over a relatively long period of time. It is of value in cleaning and deodorizing chronic necrotizing wounds and sloughing ulcerating malignancies, although it should not be employed in the treatment of acute infections. The foul exudates characteristic of gangrenous infected tissues contain reduced sulfur compounds, which are selectively oxidized and deodorized by Azochloramid, other exudates or secretions being little affected by the drug. Azochloramid consequently retains its deodorizing effect for more than twenty-four hours, while chloramine-T and Dakin's solution, which attack not only the unsaturated compounds but all the other wound exudates as well, lose their effect more rapidly and exhibit a more irritative effect. Azochloramid is antiseptic and, because of its prolonged activity, serves to clear up the existent infection in a chronic sloughing wound as well as to deodorize the exudates.

Geschickter and Copeland<sup>16</sup> advise its use as follows: The affected area is soaked with hot wet dressings or in a hot bath for fifteen to thirty minutes, and six or eight layers of gauze soaked with Azochloramid in triacetin (1:500) are applied. The dressing is covered securely with rubberized silk and left in place for twelve to twenty-four hours. If the necrotic area is extensive, such dressings can be maintained continuously until a clean granulating surface results.

Azochloramid is used also in 1:3,300 solution in sterile distilled water or normal salt solution for irrigation of sinuses, infected wounds, and empyema cavities.

Zinc peroxide ( $ZnO_2$ ) was introduced by Johnson and Meleney<sup>20</sup> for treatment of chronic progressive burrowing ulcerative lesions due to persistent infections with anaerobic or microaerophilic hemolytic streptococci. The compound is nonirritating and liberates oxygen at a constant rate over a period of more than twenty-four hours. Properly used, it has a specific effect in curing infections of this type, although it is of little use in treatment of infections due to aerobic organisms. Johnson and Meleney<sup>20</sup> state that bacteria sensitive to the action of zinc peroxide include *Streptococcus hemolyticus* (aerobic, anaerobic, and microaerophilic forms), pneumococci, vegetative forms of all the clostridia, and various anaerobic nonsporulating bacteria such as *Bacillus fusiformis*. Bacteria resistant to the action of zinc peroxide include *Streptococcus viridans*, *Staphylococcus aureus*, *Escherichia coli*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, and spores of all types.

Cultures must be taken from sinuses in the infected area or from beneath the undermined skin edges, planted on the usual media, and incubated both in aerobic and anaerobic environments. Since the organism is an ordinary hemolytic streptococcus which has become adapted to an anaerobic environment, it will show the cultural characteristics of the original organism as well.

Zinc peroxide is of value only when it can be brought into direct contact with the infected area. If the streptococcic infection is a diffuse cellulitis, penicillin or sulfadiazine administered systemically is the treatment of choice. If areas of localized necrosis or collections of pus are present, surgical drainage is of paramount importance. When the lesion is a chronic burrowing necrotizing ulcer, however, zinc peroxide should be applied locally in combination with the proper chemotherapeutic agent administered orally or parenterally.

The method of application is of importance; unless the proper procedure is followed in detail, satisfactory results will not be obtained. Before use, zinc peroxide must be activated by dry sterilization in relatively small quantities at 140° C. for four hours. The powder then is mixed thoroughly with an equal quantity of sterile water in a sterile medicine glass immediately before each application to form a suspension as thick as heavy cream. The wound is sponged with sterile normal salt solution and the fresh suspension thickly applied by means of a blunt syringe,

particularly into the sinuses and beneath the undermined skin edges, which should be opened up surgically if necessary. Complete contact must be achieved with all parts of the infected surface. When the entire wound has been coated thoroughly with the creamy suspension, several layers of fine-meshed gauze soaked in the zinc peroxide preparation are applied and the area is covered with petrolatum gauze or rubberized silk to prevent evaporation and drying. The dressing is changed daily, the wound being cleaned with sterile normal salt solution at this time. No attention to the dressing is necessary in the interval between applications.

Zinc peroxide may be used effectively also as a local application and mouthwash in certain anaerobic infections of the oropharynx (p. 202).

*Acetic acid* is sometimes of value in treatment of wound infections due to *Proteus vulgaris* or *Pseudomonas aeruginosa*. No specific agent effective against these bacteria is generally available at present; acetic acid occasionally discourages their growth by rendering the pH of the environment unfavorable. Acetic acid is used for this purpose in concentrations of 0.5 to 1.0 per cent in sterile distilled water and is applied as constant wet dressings which are completely changed at least once a day. If the infection has not disappeared within three to four days, further use of acetic acid probably will be of no value and may cause maceration and necrosis of the wound edges. The best method at present for clearing superficial wound infections due to gram-negative bacteria is by use of dry fine-meshed gauze and pressure dressings changed at least once and preferably twice daily.

*Urethane*, applied in 10 per cent solution as continuous wet dressings, is reported<sup>21</sup> to be effective in eliminating gram-negative organisms from mixed wound infections; urethane-penicillin mixtures should prove even more useful.

Digestants are of service occasionally for removal of large necrotic sloughs. The best way to clean necrotic tissue from a wound is by surgical excision; however, it is possible that this may be unwise at times if infection is extensive, the slough is widespread, and the patient is in poor general condition.

*Pyruvic acid* is perhaps the most powerful digestant available at present; Connor and Harvey<sup>22</sup> have reported its use for the removal of extensive deep sloughs in severely burned patients.

Following application of pyruvic acid paste locally, the sloughs separate within seven to ten days without damage to viable tissue, leaving a clean granulating surface immediately acceptable for grafting or other operative procedures. Separation of the slough is believed to be due to reduction of the pH on the surface of the wound.

Pyruvic acid paste is made from a stock solution prepared by the addition of 7 c.c. of pyruvic acid to one liter of distilled water, the pH of the resulting solution being about 1.9. From this, the approximate amount necessary for the dressing is taken and is divided into two portions, one of which is four times the volume of the other. The smaller portion is mixed while cold with half its weight of cornstarch. The larger portion is heated to just below boiling and then is mixed while hot with the cold starch paste. After mixing, the paste is cooled in an ice bath.

The paste is applied thickly to the sloughing area, which may be incised at intervals to permit penetration of the paste. A thin layer of fine-meshed dry gauze is applied and the entire area is covered with petrolatum gauze to prevent drying. A bulky gauze dressing is applied and fixed with adhesive tape or, if possible, with a woven elastic bandage. Dressings are changed every two to three days, similar applications of pyruvic acid paste being made each time.

*Allantoin*, an oxidation product of uric acid, is occasionally of value in the treatment of necrotic, sloughing wounds which are slow to heal and which exhibit no active inflammation. Allantoin can be used in 0.5 per cent solution in sterile distilled water or normal salt solution as constant wet dressings or as a 2 per cent ointment for periodic topical applications. *Urea crystals*, applied directly to a deep sloughing wound after sponging with normal salt solution, also are said to be of benefit. *Dakin's solution*, a chemical digestant, employed with excellent results during and after World War I, is little used at present because other methods provide equally good results and require less time and attention.

Growth-stimulating substances are applied to the surfaces of indolent wounds to promote more rapid healing. *Balsam of Peru* and *scarlet red ointment* are perhaps the most widely employed of the older medications used to stimulate epithelial growth. The water-soluble derivatives of *chlorophyll*, applied either in aqueous solution or in a hydrophilic ointment (1 per

cent), have been used to stimulate growth in indolent ulcers, to control chronic surface infections in wounds, and to minimize the odor from sloughing infected lesions.

*Cod-liver oil* has been advocated as a stimulant to healing; it may be applied liberally to the wound either as the pure oil or as an ointment (25 per cent) made with sterile petroleum jelly. When cod-liver oil is used, dressings should be changed infrequently. Its value as a local application, however, is open to question.<sup>23</sup> *Red blood cells*, left as a by-product after the plasma has been separated from over-aged bank blood, may be applied<sup>24</sup> daily to indolent wounds, either as a powder or incorporated in an ointment. Healing of chronic open lesions may be stimulated in some cases by repeated application of *amino acid* solutions or, perhaps better, of powdered casein to the wound surface.

Increased rate of healing is attributed frequently to the effect of substances applied to the wound; it is probable that in most cases the improvement is due at least partly to systemic correction of nutritional deficiencies, to systemic administration of antibacterial substances, or to correction of the fundamental causes which produced the lesion. However, it cannot be denied that in some cases indolent uninfected wounds and ulcers appear to heal more rapidly following continued application of protein substances such as those mentioned.

Hemostatic substances are used to stop the flow of blood from a bleeding surface by inducing prompt formation of a strong clot. Whenever possible, use of a suture or a ligature is to be preferred; a tied vessel is less likely to bleed again than is a vessel plugged by a clot. However, in many cases, application of a suture or ligature is impossible because of the nature of the bleeding tissue or extent of the bleeding surface.

Until recently, no dependable local hemostatic agent was available and persistent bleeding had to be controlled by insertion of a dry gauze pack. Such packs must be removed later and always cause pain and usually cause renewed bleeding when withdrawn. Other well-known but undependable hemostatic agents include bits of muscle tissue excised from a nearby area and fixed in contact with the bleeding point, epinephrine (1:1,000) solution applied by means of a sponge pressed to the oozing surface, and moist heat applied by pressure with a hot wet gauze pack. Chemical agents which occasionally are effective in capil-



lary oozing include thromboplastin (cephalin) extracts, solid silver nitrate (lunar caustic), and ferric chloride solutions.

Within the past few years, several hemostatics have been developed which are safe for clinical use, are absorbed from the tissues without interference with function or formation of scar, and will stop even brisk capillary or venous bleeding promptly and dependably.

*Gelatin sponge*, introduced by Correll and Wise,<sup>25</sup> is a foam-like product composed of gelatin which can be cut into pieces of any desired size and shape either in the dry state or when wet. It is easy to handle, inexpensive, and rapidly effective. Gelatin sponge absorbs liquids readily and is best used with thrombin solution or normal salt solution. Although thrombin solution adds to the hemostatic effect and therefore always should be employed, gelatin sponge wet simply in normal salt solution is promptly effective in arresting venous hemorrhage. For use, the dry sterile gelatin sponge is placed in thrombin or saline solution for a minute or more and then is cut into the size desired. The bleeding point is cleaned with a dry gauze sponge and the gelatin is applied and pressed firmly against the site of hemorrhage for two to four minutes. Pressure is released and the sponge is allowed to remain in place. Suture fixation may be used if necessary. It is believed that release of thrombin occurs when the patient's blood platelets come into contact with the large surface area afforded by the cells of the gelatin sponge and that fibrin formation immediately results. Obviously, if thrombin solution is used also, fibrin precipitation will be even more prompt. The sponge is quickly bound to the bleeding point by formation of the clot and should not be removed. Experimental and clinical studies<sup>26</sup> have shown that gelatin sponge is absorbed completely in from one to five weeks, leaving little indication of its location. Although much more valuable for use during the course of operative procedures (biliary tract surgery, neurosurgical procedures,<sup>27</sup> thoracic operations, etc.), gelatin sponge wet with thrombin solution is promptly effective in controlling postoperative bleeding from accessible surfaces which cannot be sutured.

*Fibrin foam*, prepared from human blood plasma, has been advocated by Ingraham and Bailey<sup>28</sup> for use in combination with thrombin solution as a topical hemostatic agent. For use, the fibrin foam is soaked for a minute or more in thrombin solution

and then is pressed against the site of hemorrhage for several minutes. Indications for use and degree of effectiveness are the same as for gelatin sponge; capillary and venous bleeding are controlled promptly and effectively and the fibrin foam is absorbed completely by the tissues in from one to four weeks.<sup>29</sup> Fibrin foam does not take part in stimulation of coagulation; it serves as the matrix for the thrombin solution, which initiates clotting by causing precipitation of fibrin strands.

*Oxidized cellulose* or cellulosic acid (absorbable gauze), investigated experimentally and clinically by Frantz and Lattes,<sup>30</sup> resembles ordinary gauze or cotton in appearance,<sup>31</sup> consistency, and method of handling. Unlike ordinary gauze, it can be packed into a bleeding wound to secure hemostasis and can be left without necessity for removal, since it is absorbed by the tissues within a period of several weeks. Absorbable gauze is used only as a hemostatic agent; it is used in the dry state and is simply packed against the bleeding area. Sutures may be used to hold it in place if necessary. As soon as the gauze becomes saturated with blood, it swells and becomes a sticky dark brown or black mass, causing hemostasis by acting in place of a clot. The mass of gauze is firmly fixed and difficult to remove after twenty-four hours, although it is soft and gelatinous after two days and then can be scraped off gently if desired. Thrombin cannot be used together with absorbable gauze; the acid reaction of the oxidized cellulose renders thrombin inactive, and if an alkaline solution is added to activate thrombin, it renders the gauze ineffective.

Other hemostatic substances, such as sodium and calcium alginates,<sup>32</sup> are being investigated and apparently offer some advantages. The latter compounds, which are not yet available generally, are prepared by hydrolysis of certain types of seaweed and apparently can be processed to form a gel, a foam, a film, or even a gauze resembling surgical gauze.

### Drains

Under certain circumstances, drainage is instituted in surgical wounds either to prevent the development of infection or to allow the escape of exudate or secretion.

Drains are of several types, depending upon the purpose to be accomplished. Fine meshed gauze, either dry or impregnated

with emollients, is used as packing in contaminated or traumatic wounds that cannot be sutured. Rubber sheeting (rubber dam) is used in small strips to drain areas of superficial infection or sutured wounds that may develop collections of serum. Larger strips, or even rolled tubes (Penrose drains), are used to drain wounds that can be closed but are likely to develop infections; for example, laparotomy incisions in patients with suppurative appendicitis, gangrenous cholecystitis, or perforated peptic ulcer. Cigarette drains (Penrose tubing containing dry gauze) are used for drainage of peritoneal abscesses and infections, such as the localizations of pus which occur in patients with spreading peritonitis. Rubber tubes are used either for drainage of a cavity with rigid walls, as in empyema, or for insertion into a viscus such as the gall bladder or a portion of the gastrointestinal tract. In the latter case, the tube is fixed to the wall of the viscus by a water-tight closure. Rubber tubes are never used for drainage of the peritoneal cavity; pressure of the hard tube against a viscus or a blood vessel may cause erosion and perforation. Similarly, raw gauze is never used for drainage in any deep wound; too much trauma is caused by its removal and if a suture line is nearby, the gauze may become adherent to the sutured area.

Penrose tubing or cigarette drains when used in the peritoneal cavity can drain only the area immediately surrounding the drain itself; there is no possible way to drain the entire peritoneal cavity. Because drains act as foreign bodies, they promptly evoke a local inflammatory reaction and become surrounded by a layer of plastic fibrinous peritoneal exudate. Organization of the exudate follows quickly and the drain or tube is effectively separated from the peritoneal cavity by a thick layer of fibrinous adhesions closely applied to the viscera or structures around the tube. As a result, drains do not actually drain an area but cause it to be walled off from the peritoneal cavity by promoting the formation of limiting adhesions. As long as the drain is in place, purulent exudate or fluid discharged from the drained area is conducted out to the abdominal wall; when the drain has fulfilled its function and is removed, the long sinus tract collapses and promptly grows together, obliterating the channel.

Following operations upon the biliary tract, Penrose or cigarette drains are placed down to the subhepatic space by many surgeons to permit escape of bile-stained exudate or even of bile

itself. Other surgeons consider drainage unnecessary in these cases. After drainage has been established in pelvic or subphrenic abscesses, Penrose drains will prevent or at least minimize reaccumulation of pus. Use of Penrose drains following removal of a suppurating or perforated appendix is a debated question (p. 649); when used in such cases, drains permit escape of purulent exudate from the appendicocecal region and, more important, cause this area to become walled off from the rest of the peritoneal cavity.

While drains are indispensable when their use is indicated, improper use may cause harm. Drains are foreign bodies and in the presence of infection act as infected foreign bodies. Neither complete subsidence of infection nor proper healing will occur if drains are allowed to remain too long in an infected wound; the formation of infected granulation tissue is stimulated, excessive scar tissue is produced, and subsequent wound healing is weakened. Drains will produce pressure necrosis if placed in contact with viscera or with tissues of low vascularity; fecal fistulas may result from pressure against bowel, and tendon sloughs will develop from contact with tendons. Gauze will adhere to a ligature or to a sutured area; no gauze should be allowed to protrude from the deep end of a cigarette drain placed in the abdomen, nor should the end of a drain be allowed to touch the site of operative repair.

Drains evoke the formation of granulation tissue and of adhesions when placed in contact with any serous surface, whether tendon sheath, pleural cavity, or peritoneal surface. Drains placed in the peritoneal cavity are never allowed to touch small bowel; the drains always are carried along the lateral peritoneal walls, above the transverse colon, or through the cul-de-sac from below, to minimize the formation of adhesions between loops of small intestine. Such adhesions are likely to produce mechanical intestinal obstruction either immediately or at any subsequent time. Because of the possibility of producing a weakened area in the incision, it is preferable not to bring abdominal drains or tubes through the wound but to make a small stab wound for this purpose.

Except in the case of rubber tubes, the flow of exudate along a drainage tract occurs on the surface of the drain, aided perhaps by capillary attraction, rather than through it. For this

reason, a single cigarette drain may act as a plug when the wound is closed tightly; two drains are much more effective and occupy little more space than one.

Drains occasionally drop back into the wound and are lost, requiring operative removal. This accident may occur with a large thoracotomy tube as well as with a small rubber incisional drain. The end of each drain used must project several centimeters beyond the skin surface; if more than one drain is used, the end of each must be visible and easily accessible. Dressings should never be applied either in the operating room or on the ward until each individual drain has been transfixed with a sterile safety pin and, in some cases, fixed to the skin with a silk suture. If the pinned drain is lost, a plain x-ray will show at once whether it was removed unnoticed with the dressing or lost in the depths of the wound.

The proper time for removal of drains is decided by the surgeon in each case. Usually, drains used simply for prevention of soft tissue infection are removed after two or three days, while drains used following evacuation of soft tissue infections are withdrawn as soon as cellulitis has disappeared and collections of exudate have been cleared away. Drains used in cavities with rigid walls, such as empyema cavities, are withdrawn gradually and are removed entirely only after the cavity has filled with granulation tissue. Drains placed in the abdominal cavity are taken out when the acute infection has subsided, when the drained area is well walled off, or when the danger of leakage from a sutured area has passed.

Removal of a drain is accomplished gently; if difficulty is anticipated, the patient should be given morphine, 10 to 16 mg. (gr.  $1/6$  to  $1/4$ ), or an equivalent dose of another sedative a few minutes before the dressing is changed. The drain is grasped near the wound with a sterile clamp, twisted slowly to free it throughout its length, and withdrawn gently with a twisting motion. Once a drain has been removed, it cannot be reinserted; if its period of usefulness has not ended or if the drainage tract is long and deep, it may be advisable to withdraw it over a period of two or three days rather than at once. As a rule, however, complete removal of a drain is preferable to successive shortening. In every case, it is imperative to note on the chart, with the date and the signature of the attendant, the insertion of drains at opera-

tion and the removal of drains subsequently. This precaution takes little time and may save much trouble and perplexity.

### Wound Complications

The chief complications of surgical wounds include post-operative hemorrhage, development of a hematoma or accumulation of serum, infection, delayed healing, and dehiscence. Although a sutured undrained wound usually is not dressed until time for removal of sutures, the wound should be examined at once if the dressings become stained with an excessive amount of exudate or blood, if systemic evidences of infection appear, or if the patient complains of constant or throbbing pain in the wound. If the wound is located on an extremity, the appearance of edema or of circulatory impairment distal to the dressing also necessitates investigation.

Postoperative hemorrhage may occur in a wound either as primary hemorrhage during the first forty-eight hours or as secondary hemorrhage after five to seven days. Moderate pain may occur locally from tension; the chief systemic indications are pallor, weakness, restlessness, rise in pulse rate, and fall in blood pressure. These evidences of hemorrhage occur only when the blood loss is moderate to severe; if they appear, red blood cell count and hematocrit determination should be made and the wound should be inspected at once (but not probed) for visible evidence of bleeding. As a rule, the first evidence of hemorrhage is the appearance of fresh blood on the dressing.

Occasionally, slight hemorrhage from the wound can be stopped by application of a pressure dressing, with administration of a transfusion if necessary. If this new dressing becomes soaked with blood, no further attempts to stop the bleeding by pressure are warranted. By no means should a dressing simply be reinforced by bulky additions placed over the original one; all that can be accomplished by this is to hide the bleeding from sight until it soaks through again.

The safest procedure is to apply direct pressure for temporary control, return the patient to the operating room, administer light gas anesthesia, reopen the wound by aseptic technique, locate the bleeding point, and secure it with a suture. After evacuation of the clot, the wound is closed without drainage. This

procedure should never be attempted on the ward; location of the point of hemorrhage sometimes is fairly difficult. If the bleeding comes from a surface which cannot be sutured, one of the hemostatic sponges (p. 490) may be applied. Large quantities of the hemostatic agents are not necessary; although they are absorbed from the tissues without residue, they act as foreign bodies when used in excessive quantities. These hemostatics are especially useful for treatment of bleeding from a tonsillar fossa or a tooth socket. Other measures which are advisable in the care of postoperative hemorrhage include determination of blood coagulation time and administration of blood transfusions either to correct a bleeding tendency or to replace excessive blood loss. Either penicillin or sulfadiazine should be administered systemically in full therapeutic dosage for from three to five days to discourage the development of wound infection.

*Hematomas* of small size and *pockets of serum*, when present, are discovered at the time of removal of sutures. These accumulations cause no signs or symptoms; their chief disadvantages are that they encourage wound infection and delay healing by creating a dead space. Treatment consists of evacuation by insertion of a sterile probe or hemostat through the most superficial area, previously cleaned with an antiseptic. A snug dressing is applied; no drains are inserted.

Wound infection is one of the commonest of postoperative complications, occurring in from 2 to 5 per cent of all patients with clean surgical wounds. Although most such infections are minor and do little more than prolong the patient's hospital stay, many of them are serious enough to be considered major complications. The organism most commonly found<sup>22</sup> in infections of clean surgical wounds is the staphylococcus, while the streptococcus ranks next in rate of incidence. Infection of this type is due not to the introduction of bacteria during the postoperative period but to the proliferation of organisms carried into the incision in the operating room during performance of the surgical procedure. Contaminating bacteria find their way into the wound from the skin, which can be cleaned but not sterilized before operation, from the hands and the respiratory tracts of the surgeon and his assistants, from the instruments, from the air, and, in some cases, from the field of operation itself. While it is not possible to eliminate wound infections entirely, it is quite possible to reduce

their incidence to a low figure; the percentage of wound infections developing after operation depends to a great extent upon the surgical technique of the operator.

Precautions to be taken in the operating room are familiar to every surgeon and include particularly the observance of the principles of asepsis, use of sharp dissection, minimal handling of tissues, protection of the wound edges and surfaces, gentle manipulations, avoidance of clamping or ligating large portions of tissues, and conservative use of fine suture material tied snugly but not tightly. Insertion of drains into the peritoneal cavity in the presence of infection is a matter to be decided by the individual operator; there is much disagreement on this point. In any case, however, it is advisable to leave a small drain down to the closed peritoneum when contamination of the incision has occurred; for example, in operations for removal of a suppurating appendix or gangrenous gall bladder or for closure of a perforated peptic ulcer. Such a drain can be removed after two or three days; the danger of wound infection is minimized without interference with wound healing or weakening of the scar. Use of sulfonamides locally in such wounds is of little or no value, although systemic chemotherapy is certainly indicated. Following operations of this type, closure of all layers of the wound except the peritoneum should be made with interrupted sutures to permit seepage of infected exudate to the surface without disruption of an entire suture line.

Wound infections are especially likely to develop in debilitated patients, whose general resistance is depressed, or in obese patients, whose tissues are infiltrated with fat and therefore have a low resistance to infection. Clinical evidence of wound infection appears from three to six days after operation and is usually indicated by a rise in temperature, often with no other symptoms, either local or general. Fever from this cause characteristically is low grade and irregular, persisting until the infection localizes and is drained, although the onset of the febrile reaction occasionally is sudden and abrupt. During the stage of early cellulitis in the deeper layers of the wound, little or no evidence of infection may be visible externally. As inflammation progresses and the amount of exudate increases, the wound becomes painful and somewhat swollen.



When incisional infection is suspected, the dressings are removed and the edges of the wound palpated. For proper protection, the operator should wear sterile gloves and apply an antiseptic solution to the wound area before palpating. No instrument should be introduced into the wound unless evidence of an infection is present; if the wound appears clean and no localized tenderness is present, the dressings are replaced. Examination twelve hours later will show conclusive evidence of infection if the fever is due to this cause.

For drainage of a wound infection, an antiseptic is applied, one or two of the skin sutures are removed, and a probe is introduced at the point of maximum tenderness. The collection of pus is evacuated through a tract made by insertion of a sterile clamp. Cultures are taken, enough skin sutures are removed to insure an adequate outlet, and systemic chemotherapy is begun. A small drain may be inserted for a day or two. Hot wet dressings are not used unless the infection is superficial; heat from such a source will not penetrate to the deeper layers and the moist dressings may cause maceration around the skin sutures. If the response is not prompt and satisfactory, the wound is explored again and more efficient drainage is secured. Identification of the infecting organism by smear and culture will indicate the type of systemic therapy best suited; gram-positive organisms respond best to penicillin or sulfadiazine, while gram-negative bacteria require the use of streptomycin. Local chemotherapy is not indicated during the acute stage of postoperative wound infection; manipulations of the wound are restricted to those necessary to secure free drainage. Introduction of syringes, instruments, or solutions is likely to add secondary contaminants to the infecting bacteria already present.

A persistent wound infection is due occasionally to the presence of a retained foreign body such as a fragment of gauze or a broken rubber drain.

Delayed healing of wounds is manifested either as failure of an apparently uninfected wound to unite within the expected time or as failure of a wound infection to respond properly to adequate treatment, with persistence of a granulating cavity and growth of a mixture of bacteria on its surface.

As stated previously, deficient wound healing may be caused or favored by the presence of anemia, dehydration, tissue edema,

hypoproteinemia, malnutrition, and avitaminosis and by the presence of such contributory conditions as uncompensated heart disease, severe diabetes, significant arteriosclerosis, or advanced age. Local causes of delayed healing include communication of the wound with a viscus with fistula formation, the presence of persisting infection, necrotic tissue, or foreign bodies, the effect of excessive trauma or of insertion of tight and excessive sutures at operation, the separation of the wound edges by a hematoma or accumulation of serum, excessive motion or activity of the injured part, and failure of a normal healing response.

Ordinarily the cause for failure to heal is obvious. It is worth noting, however, that a subacute or chronic infection which appears to be the factor impeding wound repair may continue only because the patient is debilitated and unable to cope with the bacterial growth. Since delayed healing is more often due to a combination of causes than to a single one, routine laboratory investigations for study of this condition should include identification by smear and culture of the organisms on the wound surface, red blood cell and leucocyte counts, hematocrit determination, estimation of plasma protein concentration, estimation of vitamin C level of the plasma or of the urine, routine urinalysis, and measurement of the daily total urinary output. If laboratory facilities are not available, administration of a high dietary protein intake, therapeutic doses of vitamin B complex and ascorbic acid, and, if possible, transfusion of blood will always accelerate the process of healing toward a more nearly normal rate.

Dehiscence or disruption of the laparotomy wound is one of the most disturbing accidents of the postoperative period. Not only is the patient's convalescence interrupted and prolonged, but a second and unexpected major operation is necessary, which is distressing to the patient and his family as well as to the operator. The incidence of wound disruption in patients with clean wounds averages less than 1 per cent, but the mortality is high, varying from 20 to 40 per cent.

The basic cause for wound dehiscence has never been defined, although many contributory factors have been recognized. The same systemic conditions which interfere with wound healing also will act as contributory causes to wound disruption; namely,

cachexia due to chronic visceral disease or to malignancy, anemia, advanced age, hypoproteinemia, dehydration, toxemia due to infection, severe systemic disease such as cardiovascular disease or diabetes, and possibly avitaminosis C. The exact part played by each of these states is debatable and wide disagreement exists among those who have studied the subject. One point of view which is generally accepted is that of Koster and Kasman,<sup>33</sup> who state that while hypoproteinemia *in itself probably is not a sufficient cause for wound disruption*, it indicates a poor nutritional state which may favor wound disruption.

Local factors which act as contributory causes to wound dehiscence include defective or improper suturing of the abdominal incision, the use of bulky drains through the incision, the presence of local infection or necrotic tissue in the wound, and the occurrence of postoperative strain due to prolonged abdominal distention or to excessive vomiting, retching, coughing, or hiccough. Some observers feel that wound disruption may be due to rapid absorption of catgut sutures in certain patients because of an allergic reaction and that all closures, at least above the peritoneal layer, should be made with silk.<sup>34</sup> Others maintain that wound disruption is due to an interference with the healing process itself and that the suture material used is of little importance. Maes and associates<sup>35</sup> state that catgut used with "silk technic" is as safe as silk; Fallis<sup>36</sup> also believes that the cause of wound rupture lies in failure of healing rather than in faulty suturing. Pickrell and Clay<sup>37</sup> were unable to find any evidence experimentally that catgut is capable of producing an antigenic response in the tissues.

Disruption of abdominal wounds may occur from the second to the fourteenth day after operation, although it is most common from the sixth to the eighth day. This complication usually appears in a patient who has run a disturbed postoperative course, marked by continued elevation of temperature and of pulse rate, prolonged intestinal distention, persistent nausea and vomiting, or a poor response in general. The best and most dependable early evidence of wound dehiscence is the *profuse* drainage of a pink-stained serous exudate from the wound. Occasionally the patient will sense that something has happened to his incision; either this complaint or the unexpected drainage

of watery fluid from the incision demands immediate careful inspection of the wound under sterile precautions. A soft non-inflammatory swelling may be visible beneath the incision, perhaps with a small opening from which serous fluid can be expressed. The entire region should be cleaned with an antiseptic and investigated with a sterile clamp to ascertain whether the collection of fluid is simply a small postoperative accumulation or whether it represents a beginning disruption.

Such serous drainage may be followed either immediately or after a day or two by widespread disruption of the wound. In such cases, removal of the dressing will reveal gaping of the incision, either totally or in part, with omentum and loops of small bowel lying free on the abdominal wall and in the depths of the separated wound. Complete disruption is more common in lower abdominal wounds; partial separation is more often seen in upper abdominal incisions, although any degree of dehiscence may occur in either location.

Treatment of wound dehiscence at any stage consists of immediate application of a sterile towel over the wound until emergency secondary closure of the incision can be done. Secondary suture is performed in the operating room under local anesthesia, supplemented if necessary with light gas anesthesia. No attempt is made to close the wound in layers; the best procedure is the introduction of interrupted heavy silver wire sutures (20 to 22 gauge), passing through all layers of the abdominal wall on both sides (Fig. 53). These sutures are placed sufficiently close together to prevent later herniation of omentum or small bowel between the sutures. Silver wire may not be sufficiently strong for use in obese patients; kangaroo tendon may be preferable in such cases. When wound disruption occurs in a patient who is too profoundly ill to withstand this surgical procedure, the operator should scrub his hands, put on sterile gloves, clean the abdominal wall with antiseptic without allowing the solution to touch the herniated viscera or open wound, and replace the protruding abdominal contents into the peritoneal cavity gently. Following this, the abdomen is painted with compound tincture of benzoin and the wound edges are brought together as completely as possible by means of strips of flamed adhesive tape. Additional strips are applied several hours later if necessary to

secure complete approximation. Operative closure should be done whenever possible, however.

In any case, whether the patient is treated by operative closure or by adhesive strapping, gastrointestinal suction drainage is instituted with a Wangenstein apparatus or, preferably, a Miller-Abbott tube. Transfusion of blood is always of value and may well be administered even before red cell counts or hematocrit studies are made. Large doses of vitamin C, at least 500 mg. twice daily, are supplied and administration of sulfadiazine or penicillin is begun in full therapeutic dosage. Efforts are made to supply a high dietary protein intake either orally or parenterally in accordance with the patient's condition.

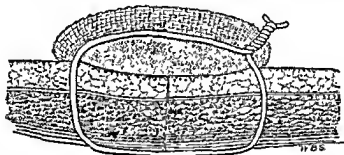


Fig. 53.—Wound dehiscence. Closure is effected by silver wire (22 gauge) sutures through all layers of the abdominal wall.

Disruption occurs most often during the lag period of wound healing. If the patient survives the secondary closure, healing of the incision proceeds promptly and without incident, firm union occurring in little more time than if disruption had not developed. For added safety, however, the massive sutures are allowed to remain for at least fourteen days following insertion; some surgeons prefer to leave them for three weeks. While the incidence of wound disruption may be lowered by careful preoperative preparation and by proper surgical technique, occasional cases still will occur. Reduction in mortality rate can be effected by watchfulness and by prompt recognition of the signs indicating impending or early disruption. The unexpected outpouring of thin serous fluid from a clean laparotomy wound near the end of the first postoperative week is the most dependable early indication of this complication.

Gas gangrene, usually a sequel to traumatic wounds characterized by destruction of muscle tissue, is seen occasionally as a complication to intraperitoneal leakage from the large bowel. The disease is caused by certain members of the clostridia; although about twenty organisms have been classified in this group of gram-positive spore-forming anaerobic bacteria, only five<sup>28</sup> are capable of producing clinical gas gangrene. *Clostridium welchii* (*Bacillus perfringens*) is by far the commonest offender and is the one which characteristically produces gas in the tissues; *Clostridium novyi* (*Bacillus oedematiens*), *Clostridium septicum* (*Vibrio septique*), *Clostridium sordellii*, and *Clostridium histolyticum* are the other pathogenic clostridia and typically produce a profound and rapidly spreading edema. Clostridia are normal inhabitants of the intestinal tract both in man and in animals; the spores can live for years under the most adverse circumstances, being completely destroyed only by heat sterilization. The pathogenicity of these bacteria is due chiefly to the elaboration of powerful exotoxins, formed in large quantities as the organisms grow and multiply, and absorbed into the general circulation.

Because clostridia occur in the intestinal tract and because they are peculiarly able to survive destructive influences, they are generally found in street dust, farm soil, road dirt, and even in clothing made from sheep's wool. The contamination of wool clothing with clostridial spores resistant to dry cleaning and pressing, as demonstrated by Maes,<sup>29</sup> may explain why war injuries occurring during the winter are more likely to be followed by gas gangrene than similar injuries incurred during warm weather. Presence of the clostridia in the bowel obviously explains the occasional occurrence of gas bacillus infection in patients with perforating injuries of the colon, gangrenous appendicitis with perforation, and even following colonic surgery as for carcinoma. Gas gangrene also may develop after amputation of an extremity for peripheral vascular disease and as a complication of infected abortion.

Clostridia frequently are found as contaminants of traumatic wounds, yet only rarely cause clinical infection. Wounds most likely to develop gas gangrene are those with extensive necrosis of muscle tissue and with recesses and pockets conducive to growth of anaerobic organisms; for example, com-

pound fractures or extensive crushing lacerations with circulatory impairment and gross contamination, especially if a tourniquet has been used or surgery has been delayed. The lower extremity and the buttock are the commonest sites; the upper extremity, back, and abdominal wall are less frequently involved. Other saprophytic organisms are capable of causing mild localized infection<sup>40</sup> under such circumstances, with production of gas bubbles and acute inflammatory reaction, yet with little evidence of toxicity and with little tendency to spread. Such infections appear from four to six days after injury and, although accompanied by gas formation, are not due to the highly pathogenic clostridia and are treated only by the usual measures for moderate tissue infections.

Gas gangrene is characterized by rapid onset of extreme systemic toxicity and by severe pain and swelling in the infected area. These symptoms develop and progress rapidly, sometimes reaching fulminating proportions within six to twelve hours after injury, and usually appearing no later than seventy-two hours after infection. The patient's general condition deteriorates rapidly to a state approaching profound shock, with a rapid running pulse, a temperature level varying from moderate elevation to a subnormal figure, and extreme weakness, exhaustion, and pallor. Mental clarity remains unaffected in some cases; the patient may be perfectly alert, anxious, and apprehensive. The infected areas and perhaps even the entire extremity are painful, tender, and swollen, with a thin odorous brownish watery discharge containing large numbers of the responsible clostridia; the surrounding skin is yellowish, with purple and greenish splotches of discoloration. The involved muscle tissue is swollen and is brick-red in color with an obviously altered and necrotic appearance.

Gas gangrene should be suspected at once in a patient with a compound fracture or a wound involving muscle if local pain, systemic toxicity, and a rapid running pulse out of proportion to the temperature elevation develop within forty-eight hours after injury or operation. Clinical confirmation of the diagnosis requires inspection of the wound and there must be no hesitation or delay in removing dressings or casts if gas gangrene is suspected. In many cases, the diagnosis will be obvious at a glance; in others, the presence of gas palpable in the tissues or visible on

plain x-ray will confirm the impression. Final diagnosis can be made only by cultural identification of the causative organisms from the wound exudate or from muscle tissue removed surgically; a rapid method for identification of *Clostridium welchii* within a period of several hours has been suggested by Heller and associates.<sup>41</sup> The presence of gas and localized swelling in the wound does not necessarily indicate gas gangrene; the presence of these signs together with pain in the wound and general toxicity usually does. Leucocytosis is present in most cases but may be absent; profound anemia develops rapidly, and jaundice may occur as a terminal event.

*Prophylaxis* depends upon proper débridement of the traumatic wound with excision of all devitalized tissue, unroofing of all crevices and extensions of the wound, removal of all contaminating dirt and foreign bodies, and avoidance of primary closure in such cases. Patients with wounds especially likely to be followed by gas gangrene may be given polyvalent gas bacillus antitoxin (10,000 to 20,000 units) intramuscularly after testing for serum sensitivity. Tetanus antitoxin or toxoid (p. 508) is given routinely at the same time under these circumstances.

Successful *treatment* of the established disease depends upon prompt recognition and immediate energetic therapy. Since the infecting organism spreads along muscles and between fascial planes in both directions, the wound must be opened widely throughout the length of the involved area and at least several inches beyond into apparently normal tissue. Fully adequate drainage must be supplied not only for the obviously infected region but also for the surrounding tissues into which the disease is spreading. Muscle tissue affected by gas gangrene is pink to brick-red in color, opaque in appearance, and swollen, noncontractile, and avascular; all muscular and fascial tissue which gives even a suggestion of being involved must be excised completely. *Cultures are taken for identification of the causative organism.* All recesses of the wound are laid open and fascial compartments in the wound area are split widely to relieve tension, prevent circulatory impairment, and allow aeration. After hemostasis is secured, the entire wound surface is treated with zinc peroxide (p. 486) and plaster splints are applied to maintain immobility. In some cases, the infection extends so rapidly that nothing less than amputation of an entire extremity will serve to halt its spread.



Therapeutic doses of polyvalent gas bacillus antitoxin are given as soon as the clinical diagnosis is made. An initial dose of 30,000 to 50,000 units is given intravenously or intramuscularly after testing the patient for sensitivity to horse serum; a similar dose is given four hours later with additional doses as indicated at six- to twelve-hour intervals. The value of antitoxin has been questioned<sup>42</sup> by some authorities and confirmed<sup>43</sup> by others; it is probable that the use of antitoxin has little effect on the ultimate mortality rate since the medication affects only the circulating toxin and does not hinder the proliferation of the organisms. In a disease so serious, however, it is justifiable to use a medication which will do no harm and may do even a little good.

Sulfonamides are of no value locally and of questionable value systemically; the same is true to a less extent of penicillin. However, since good results have been reported by some observers with both of these drugs in experimental gas gangrene, their use may be worth while. Penicillin is preferable; it must be given in extremely large doses, such as 1,000,000 units every three hours, to be of any value.<sup>44</sup> Streptomycin is of no value.

The value of irradiation treatment in gas gangrene is also controversial. Sachs<sup>45</sup> feels that radiation is of definite value in lowering the mortality rate; in fact, to such an extent that prophylactic irradiation of all compound fractures is advocated. The same suggestion has been made also by other writers. Kelly and Dowell<sup>46</sup> report such good results with radiation alone that they feel the use of antitoxin and the practice of surgical débridement during the acute stage of gas gangrene to be unnecessary. The possibility is also raised that sulfonamide therapy and irradiation are antagonistic, so that use of sulfonamides is contraindicated if irradiation is performed. This question has not yet been raised with respect to penicillin. Other investigators have had little success<sup>47</sup> with radiation treatment, although it is probable that no harm is done by it even if no favorable response is obtained. No parallel series have yet been reported of patients with gas gangrene treated by different methods under controlled conditions. Until definite and dependable information is available as to the most effective treatment, it is probable that the best course to follow upon suspicion of the disease is to (1) secure a plain x-ray film of the area for

evidence of gas in the tissues, (2) remove the dressings and inspect the wound in the operating room, (3) lay open and débride the wound as widely as necessary, (4) institute treatment with zinc peroxide locally, and (5) administer gas gangrene antitoxin in therapeutic dosage. Irradiation therapy can be given if the infection progresses after these measures have been taken. In every case, penicillin is given in full dosage, blood transfusions are administered in appropriately large amounts, and proper fluid balance is maintained. The plan of administering prophylactic irradiation to wounds likely to develop gas gangrene is worthy of further investigation.

Tetanus is an infectious disease caused by growth in the tissues of the gram-positive anaerobic spore-forming bacterium *Clostridium tetani*. Like the organisms which cause gas gangrene, the tetanus bacillus is a normal inhabitant of the intestinal tract of man and of animals and will survive in spore form for months or years in contaminated soil or street dirt. Following introduction into a wound which favors anaerobic growth, the spores are transformed into vegetative bacilli and begin to produce the extremely powerful tetanus exotoxin which causes symptoms out of all proportion to the visible extent of infection. Once thought to travel from the wound site to the central nervous system along the nerve trunks themselves, the tetanus toxin has been shown by Firor<sup>17</sup> to be transported by the lymphatics and blood vessels. It is believed that in the tissues of the central nervous system the toxin undergoes a change (fixation) which makes it resistant to the action of therapeutic antitoxin.

Wounds likely to develop tetanus infection are those which are contaminated with dirt and which favor anaerobic growth, such as puncture wounds, crushing injuries, compound fractures, powder burns, third degree burns covered by a necrotic coagulum, and even septic abortions. Tetanus spores may be present on an open wound surface without causing the disease and may even become incorporated in the healing scar without vegetative growth. Subsequent surgical procedures upon the same area occasionally may activate the infection, with clinical tetanus resulting. In a few cases of clinical tetanus, no history of preceding injury can be obtained.

The incubation period of tetanus varies from four days to four weeks, with an average of eight to ten days. The earliest symptom usually is slight muscle spasm in the region of the wound, but this escapes notice in most cases until more obvious evidence of the disease appears. Trismus, or difficulty in opening the mouth, is more recognizable and is accompanied by increased tonus in the facial muscles and the sternocleidomastoid muscles, stiffness of the neck, and rigidity of the abdominal wall without pain or tenderness. Hypertonicity progresses to increased irritability, and painful muscle spasm may be brought on by such slight stimuli as a breeze from the window, the touch of the bedclothes, or a slight jarring of the bed. In the last stages of the disease, generalized muscular spasm and opisthotonos develop and the patient quickly becomes exhausted. Tetanus should be suspected whenever a patient has tightness of the jaws, tenderness of the facial muscles, or difficulty in opening his mouth. The diagnosis must be made on a clinical basis; the number of tetanus bacilli required to produce a lethal dose of tetanus toxin is very small and the organisms may not be found on culture.

Since the mortality of tetanus is high, averaging above 45 per cent, *prophylaxis* is always important. All patients who have wounds, injuries, compound fractures, or burns that may have been contaminated by street dirt, garden soil, exposed skin, or outer clothing should be treated by prompt cleansing of the injured area, with surgical débridement as indicated, and routine immunizing therapy. Patients previously actively immunized by tetanus toxoid are given a booster dose of 1.0 c.c. of tetanus toxoid subcutaneously; those who have never been immunized are given a dose of 1,500 to 7,500 units of tetanus antitoxin to confer temporary passive immunity, the dose depending upon the extent of contamination and the degree to which the wound favors anaerobic growth. The size of the wound is unimportant; a small puncture wound or powder burn is more likely to favor development of tetanus than a huge open laceration. Tetanus antitoxin affords passive immunity for only seven to ten days; the first dose should be given on the day of injury, at which time a notation must be made on the patient's record stating whether the dose has been given or omitted. Additional doses given at intervals of seven to ten

days will prolong the incubation period perhaps until the wound has healed and conditions are less favorable for growth of the bacilli. Because spores may persist in scars, it may be advisable to administer a prophylactic dose of antitoxin (or a booster dose of toxoid if indicated) to a patient requiring operative exploration of an old traumatic wound.

Before antitoxin is given, the patient is questioned concerning previous serum treatment or evidences of allergy of any kind. If a positive answer is obtained, a test for sensitivity is made by diluting 0.05 c.c. of tetanus antitoxin with sterile normal salt solution to make 5.0 c.c. (1:100 dilution) and injecting a drop of the mixture *into* the patient's skin. A positive reaction will be evidenced within thirty minutes by the appearance of a wheal surrounded by a zone of erythema. Irregular extensions from the wheal (pseudopodia) indicate high sensitivity. Desensitization may be accomplished by injection of 0.01 c.c. of tetanus antitoxin (1.0 c.c. of the 1:100 dilution) subcutaneously and doubling the dose each half hour until the entire amount has been given.

After the disease has developed, prompt *treatment* is necessary to save the patient's life. Once a lethal dose of toxin has been fixed in the central nervous system, no treatment will be of any use; and it is impossible to tell in any case how much toxin has been fixed, how much is present in the blood, or how rapidly toxin is being elaborated. Treatment is generally directed toward neutralization of toxin with large doses of antitoxin, excision of the focus of infection, and general supportive therapy.

Performance of a skin test for sensitivity and subsequent administration of antitoxin are done simultaneously with surgical débridement of the wound to avoid loss of any time. Excision of the area infected with tetanus bacilli must be wide and radical even if amputation is necessary or if extensive burn sloughs must be cut away. Zinc peroxide dressings are applied to the open wounds and are changed at least once daily. As soon as lack of serum sensitivity has been demonstrated or desensitization has been accomplished, a dose of 50,000 units of tetanus antitoxin diluted to 300 c.c. with normal salt solution is given slowly intravenously and a similar amount injected intramuscularly, as much as possible being introduced into the

tissues around the site of infection. If desensitization is necessary, it can be accomplished as just described until 10 c.c. of the serum has been given. Twenty minutes later, 0.1 c.c. of antitoxin diluted with sterile normal salt solution is injected intravenously and the dose is doubled every twenty minutes until the full dose has been given. A syringe containing 1.0 c.c. of epinephrine (1:1,000) should be ready for immediate use in case an allergic reaction occurs. Further doses of 50,000 to 100,000 units of tetanus antitoxin are given daily intramuscularly if necessary in accordance with the patient's symptoms. Intrathecal administration is potentially dangerous and of questionable value, although advocated by many authorities.

The value of antitoxin administration depends upon the promptness with which it is given; the efficacy of wound débridement is proportionate to the extent and the speed with which it is accomplished. Because of the high mortality of the disease, not the slightest delay or compromise in treatment is permissible once the diagnosis has been made.

Since the patient with clinical tetanus requires continuous care and expert nursing, he should be placed in a private room and have special nurses. The room is kept dark and quiet, no visitors are allowed, and all stimuli are reduced to a minimum. Graham and Scott<sup>48</sup> suggest very practically that a definite schedule of treatment should be outlined on an hourly timetable so that all treatments possible can be done at one time; for example, at intervals of three hours. By this plan, the patient is assured of constant rest, disturbed only at regular three-hour intervals.

Taking of an adequate diet orally is impossible; a gastric tube should be passed intranasally as soon as tetanus is diagnosed. A properly balanced high protein, high carbohydrate diet totaling 3,000 to 4,000 calories is given through the tube, together with sufficient fluids to maintain water balance and medications as needed. Oxygen is given, preferably by means of an oxygen tent, and mucus is cleared from the mouth and throat by suction whenever necessary. Atelectasis is a common complication in the heavily sedated patient; close watch must be kept for this condition and proper aeration of the lungs restored by carbon dioxide inhalations and changes of position if atelectasis is suspected.

Heavy sedation is required both to reduce muscular spasm and reflex irritability and to decrease anxiety and apprehension. Sedatives most commonly used include a long-acting barbiturate orally, such as phenobarbital, 0.1 Gm. (gr. 1½), every four hours, a slow-acting barbiturate intravenously, such as sodium pentothal or sodium amytal in amounts of 0.5 to 1.0 Gm. as needed for generalized spasm or convulsions, and Avertin rectally in amounts of 70 to 100 mg. per kilogram of body weight every eight hours as needed for sedation. Vinnard<sup>19</sup> also advocates the use of atropine, 0.4 mg. (gr. 1/150), hypodermically every six hours to promote general relaxation and to decrease tracheobronchial secretion in the heavily sedated patient, use of the Trendelenburg position to prevent aspiration of pharyngeal secretions, and administration of sulfadiazine in therapeutic doses to prevent bronchopneumonia. Penicillin, if used in place of sulfadiazine, might be given orally rather than parenterally to avoid stimulation of the patient by frequent hypodermic injections.

Curare has been tried by Adriani and Ochsner<sup>20</sup> who found the results to be unsatisfactory. Relaxation of muscular spasms could be induced for short periods of time, but the effects were transient and dangerously toxic doses were required. Almost complete curarization was necessary to afford relief from spasm, paralysis of the pharyngeal and intercostal muscles appearing as a result.

### Fistulas

A fistula may be defined briefly as an abnormal opening or channel between two epithelial surfaces; a sinus, in contrast, is a long tubular granulating channel with a single opening to an epithelial surface. Fistulas cause divergence of drainage or of secretions away from the normal course of flow; sinuses are simply long tubular chronic wounds or tissue defects.

Fistulas in general can be classified according to type, internal fistulas making an abnormal connection between two internal epithelial surfaces and external fistulas similarly connecting the lumen of a viscus or a duct with the external body surface (Figs. 54 and 55). Fistulas also may be classified according to the organs involved. Inflammatory necrosis will cause such lesions as cecal fistulas (suppurative appendicitis),

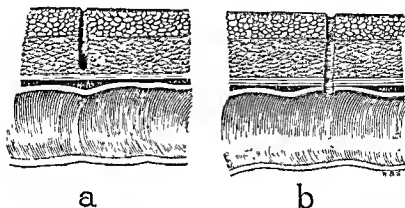


Fig 54 —a, A sinus is a simple tubular wound opening to an epithelial surface. b, A fistula is a channel connecting two epithelial surfaces. Diagram shows an external fistula between bowel and skin.

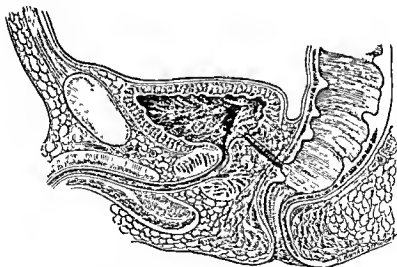


Fig 55.—Fistula between bladder and rectum is an internal fistula, connecting two epithelial surfaces within the body.

anorectal fistulas (perianal abscess), or ileoileal and ileocolic fistulas (regional enteritis). Gangrene or ulcerative necrosis is often responsible for abnormal channels such as rectovesical fistulas (carcinoma of the rectum), and trauma will produce lesions such as vesicovaginal fistula, salivary duct fistula, cerebrospinal fluid fistula, and urethral fistula. In many cases, fistulas are intentionally created surgically to sidetrack the physiologic flow of liquid or solid material from an area of which the blood supply is temporarily compromised or in which obstruction is present. For example, a fecal fistula (colostomy) sometimes is made proximal to a lesion of the colon to divert the fecal current until corrective procedures have been done and healing has occurred. Suprapubic cystostomy is performed to relieve temporarily an injured or repaired urethra from the normal physiologic burden of urine transport. Healing surgical wounds or inflammation in the common bile duct are protected by temporary external diversion of the bile (T tube drainage).

The spontaneous appearance of a fistula as a postoperative complication is always an unpleasant surprise, but it may well be a factor in saving the patient's life. Certainly the external drainage of a fecal fistula, although delaying convalescence and often even requiring later operative correction, is preferable to internal leakage from a necrotic appendicocolic area or from a suture line in damaged bowel.

Diagnosis of the type of fistula almost always can be made by examination of the discharge. Confirmation of the diagnosis is made by special tests, charcoal (4 to 8 Gm.) given orally will emerge from a fecal fistula a few hours later; phenolsulfonphthalein or methylene blue given intravenously can be detected within a few minutes in fluid drainage from a fistula of the urinary tract; and bile can be identified by appropriate tests in the drainage from a biliary fistula. It is not advisable to explore the lesion locally for a period of at least ten to fourteen days to avoid the danger of breaking through the granulating walls of the fresh fistulous tract. After this length of time, Lipiodol or Hippuran solution (aqueous) can be injected and roentgenograms taken to trace the course of the channel. Investigation with a probe or even with the finger usually adds little or no information and may be somewhat dangerous.



As a rule, the contents of a viscus or a duct will flow more readily along the normal channel than along a fistulous tract. Fecal fistulas will heal spontaneously if not too large and if no spur or obstruction exists distal to the opening. Failure of a colonic fistula to heal necessitates investigation of the reason for its persistence before operative closure is undertaken. Fistulous openings of the small bowel, however, are stubborn; persistent drainage of the fluid intestinal contents, containing powerful digestive enzymes, will cause digestion of the surface of the abdomen, rapid deterioration in general health, and interference with absorption of food. The higher the level of the fistula in the small bowel, the more prominent are the debilitating effects.

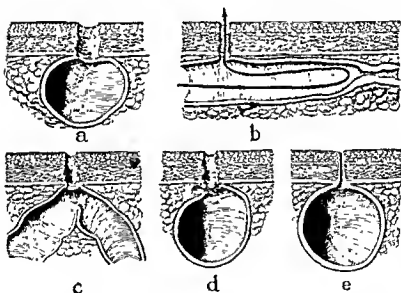


Fig 56.—Conditions interfering with spontaneous healing of fistula. *a*, short fistula with wide opening. *b*, obstruction of the normal channel distal to the fistula. *c*, presence of a spur. *d*, presence of a foreign body (e.g., heavy suture), chronic inflammation, or malignancy. *e*, epithelialization of entire tract.

Biliary fistulas heal promptly as soon as the drainage tube is removed, if the biliary ducts are unobstructed; the granulating walls of the tract unite almost at once and are quickly replaced by a thin fibrous scar. Fistulas of the urinary tract frequently require operative closure since the external opening may be

larger than the small normal drainage channel and since epithelization of the fistulous tract sometimes occurs. However, the fistula remaining after a suprapubic cystostomy tube has served its purpose and has been withdrawn will heal without difficulty, unless osteomyelitis of the pubis has developed as a complication or distal obstruction is present.

In general, spontaneous healing of a fistula will occur if the condition originally causing or necessitating its establishment has subsided or disappeared and if no factors interfering with its healing are present. Conditions which interfere with spontaneous healing of a fistula include (1) a short tract or a wide opening, (2) partial or complete obstruction of the normal channel distal to the fistula, (3) presence of a spur or angulation distal to or at the site of the fistula, (4) presence of a foreign body or of areas of necrosis or persisting inflammation, (5) presence of a granulomatous infection (tuberculosis, syphilis, or actinomycosis) or of a malignant lesion in the fistulous tract, and (6) union of the two epithelial surfaces so that the fistulous channel is lined completely with epithelium (Fig. 56).

The problems concerned in the care of fistulas, particularly with respect to the removal of drains or tubes, replacement of fluid, electrolyte, and protein losses, and protection of the surrounding skin from damage differ according to the type and location of the lesion. These considerations will be discussed in connection with the organ system involved.

### References

1. Thompson, W. D., Ravdin, I. S., Rhoads, J. E., and Frank, I. L.: Use of Lyophile Plasma in Correction of Hypoproteinemia and Prevention of Wound Disruption, *Arch. Surg.* 36: 509, 1938.
2. Wolfer, J. A., Farmer, C. J., Carroll, W. W., and Manshardt, D. O.: An Experimental Study in Wound Healing in Vitamin C Depleted Human Subjects, *Surg., Gynec. & Obst.* 81: 1, 1947.
3. Hartzell, J. B., and Stone, W. E.: Relationship of Concentration of Ascorbic Acid of Blood to Tensile Strength of Wounds in Animals, *Surg., Gynec. & Obst.* 75: 1, 1942.
4. Jones, C. M., Bartlett, M. K., Ryan, A. E., and Drummey, G. D.: Effect of Sulfanilamide Powder on Healing of Sterile and Infected Wounds, With Special References to Tensile Strength and Ascorbic Acid Content in Scar, *New England J. Med.* 229: 642, 1943.
5. Whipple, A. O.: Critical Latent or Lag Period in Healing of Wounds, *Ann. Surg.* 112: 481, 1940.

- 6 Churchill, E. D.: *Surgical Management of Wounded in Mediterranean Theater at Time of Fall of Rome*, Ann Surg. 120: 268, 1944.
- 7 DeBakey, M., and Carter, B. N.: *Current Considerations of War Surgery*, Ann. Surg. 121: 545, 1945.
- 8 Lyons, C.: *Investigation of Role of Chemotherapy in Wound Management in Mediterranean Theater*, Ann. Surg. 123: 902, 1946.
- 9 Bingham, R.: *Nonadherent Surgical Dressings*, Arch. Surg. 52: 610, 1946.
- 10 Koch, S. L.: *Care of Infected Wounds*, Internat. Abstr. Surg. 66: 105, 1938; in Surg., Gynec. & Obst. Feb. 1938.
- 11 Howe, E. L.: *Local Chemotherapy of Wounds*, Surg., Gynec. & Obst. 83: 1, 1946.
- 12 O'Donnell, C. H., Posch, J. L., and Hirshfeld, J. W.: *Study of Value of Local Sulfathiazole in Operative Wounds in Prophylaxis of Infection*, Surg., Gynec. & Obst. 82: 323, 1946.
- 13 Meleney, F. L., and Whipple, A. O.: *Statistical Analysis of Study of Prevention of Infection in Soft Part Wounds, Compound Fractures and Burns With Special Reference to Sulfonamides*, Surg., Gynec. & Obst. 80: 263, 1945.
- 14 Lyons, C.: *Chemotherapy in Management of Wounds*, J. A. M. A. 133: 215, 1947.
- 15 Meleney, F. L.: *Penicillin in the Treatment of Established Surgical Infections*, Ann. Surg. 124: 962, 1946.
- 16 Meleney, F. L., Johnson, B. A., Pulaski, E. J., and Colonna, F.: *Treatment of Mixed Infections With Penicillin, With Special Reference to Adjuvant Action of Parachlorophenol*, J. A. M. A. 130: 121, 1946.
- 17 Kozoll, O. D., Meyer, K. A., Hoffman, W. S., and Levine, S.: *The Use of Tyrothricin in Surgical Infections*, Surg., Gynec. & Obst. 83: 323, 1946.
- 18 Meleney, F. L., and Johnson, B.: *Bacitracin Therapy*, J. A. M. A. 133: 675, 1947.
- 19 Geschickter, C. F., and Copeland, M. M.: *Deodorization and Management of Fungating Wounds in Malignant Disease*, South. Surgeon 7: 244, 1938.
- 20 Johnson, B. A., and Meleney, F. L.: *Antiseptic and Detoxifying Action of Zinc Peroxide on Certain Surgical Aerobic, Anaerobic, and Microaerophilic Bacteria*, Ann. Surg. 109: 881, 1939.
- 21 Howe, C. W., and Weinstein, L.: *The Action of Urea and Some of Its Derivatives on Bacteria. IV. The Effect of a Mixture of Urethane and Sulfanilamide on the Bacterial Flora of Infected Wounds in Man*, Surg., Gynec. & Obst. 81: 913, 1947.
- 22 Connor, G. J., and Harvey, S. C.: *The Pyruvic Acid Method in Deep Clinical Burns*, Ann. Surg. 121: 799, 1946.
- 23 Williams, R. H., and Bissell, G. W.: *Effect of Topical Application of Vitamins and Some Other Chemicals on the Healing of Wounds*, Arch. Surg. 49: 225, 1944.

24. Murray, C. K., and Shaar, C. M.: Red Blood Cell Paste in Treatment of Ulcers and Chronically Infected Wounds, *J. A. M. A.* 125: 779, 1944.
25. Correll, J. T., and Wise, E. C.: Certain Properties of New Physiologically Absorbable Sponge, *Proc. Soc. Exper. Biol. & Med.* 58: 233, 1945.
26. Jenkins, H. P., Senz, E. H., Owen, H. W., and Jampolis, R. W.: Present Status of Gelatin Sponge for the Control of Hemorrhage, *J. A. M. A.* 132: 614, 1946.
27. Pilcher, C., and Meacham, W. F.: Absorbable Gelatin Sponge and Thrombin for Hemostasis in Neurosurgery, Experimental and Clinical Observations, *Surg., Gynec. & Obst.* 81: 365, 1945.
28. Ingraham, F. D., and Bailey, O. T.: Clinical Use of Products of Human Plasma Fractionation. III. The Use of Products of Fibrinogen and Thrombin in Surgery, *J. A. M. A.* 126: 680, 1944.
29. Bailey, O. T., Ingraham, F. D., Swenson, O., and Lowrey, J. J.: Human Fibrin Foam With Thrombin as a Hemostatic Agent in General Surgery, *Surgery* 18: 347, 1945.
30. Frantz, V. K., and Lattes, R.: Oxidized Cellulose-Absorbable Gauze (Cellulosic Acid), *J. A. M. A.* 129: 798, 1945.
31. Blaine, G.: Experimental Observations on Absorbable Alginate Products in Surgery, *Ann. Surg.* 125: 102, 1947.
32. Meleney, F. L.: Infection in Clean Operative Wounds, Nine Year Study, *Surg., Gynec. & Obst.* 60: 264, 1935.
33. Koster, H., and Kasman, L. P.: Relation of Serum Protein to Well Healed and to Disrupted Wounds, *Arch. Surg.* 45: 776, 1942.
34. Krauss, C. J., Kesten, B. M., and Cimiotti, J. G.: Relation of Catgut Sensitivity to Wound Healing, *Surg., Gynec. & Obst.* 66: 628, 1938.
35. Maes, U., Boyce, F. F., and McFetridge, E. M.: Postoperative Exsiccation, With Analysis of 44 Cases, *Ann. Surg.* 100: 968, 1938.
36. Fallis, L. S.: Postoperative Wound Separation, Review of Cases, *Surgery* 1: 523, 1937.
37. Pickrell, K. L., and Clay, R. C.: Wound Disruption and Catgut Allergy—Experimental and Clinical Study With Review of Literature, *Surgery* 15: 333, 1944.
38. Reed, G. B., and Orr, J. H.: Gas Gangrene, *Am. J. M. Sc.* 206: 379, 1943.
39. Maes, U.: Gas Gangrene, With Special Reference to Importance of Wool as a Source of Contamination, *Arch. Surg.* 11: 393, 1940.
40. Sewell, R. L., Dowdy, A. H., and Vincent, J. G.: Chemotherapy and Roentgen Radiation in *Clostridium Welchii* Infections, Clinical and Experimental Study, *Surg., Gynec. & Obst.* 74: 361, 1942.
41. Heller, G., Freeman, M. E., Shope, N. H., and Kindrick, R. H.: The Identification of *Clostridium Welchii* in Mixed Cultures and Debrided Tissue and Determination of Sensitivity of the Organism to Penicillin, *Surg., Gynec. & Obst.* 83: 343, 1946.

42. Monroe, C. W.: Debridement—When and How Much? Comparative Study of Battle Casualties, *Bull. U. S. Army M. Dept.* 77: 37, 1944.
43. Jeffrey, J. S., and Thomson, S.: Penicillin in Battle Casualties, *Brit. M. J.* 2: 1, 1944.
44. Altemeier, W. A., and Furate, W. L.: Gas Gangrene; Collective Review, *Internat. Abstr. Surg.* 81: 507, 1947, in *Surg., Gynec. & Obst.* June 1947.
45. Sachs, M. S.: Gas Gangrene; Collective Review, *Internat. Abstr. Surg.* 80: 411, 1945; in *Surg., Gynec. & Obst.* June 1945.
46. Kelly, J. F., and Dowell, D. A.: Twelve-Year Review of X-Ray Therapy of Gas Gangrene, *Radiology* 37: 421, 1941.
47. Firor, W. M.: Treatment and Prevention of Tetanus, Collective Review, *Internat. Abstr. Surg.* 75: 185, 1942, in *Surg., Gynec. & Obst.* Aug. 1942.
48. Graham, J. R., and Scott, T. M.: Notes on the Treatment of Tetanus, *New England J. Med.* 235: 846, 1946.
49. Vinnard, R. T.: Three Hundred Fifty-Two Cases of Tetanus, *Surgery* 18: 482, 1945.
50. Adriani, J., and Ochsner, A.: Some Observations on the Use of Curare in the Treatment of Tetanus, *Surgery* 22: 509, 1947.

## CHAPTER 16

### BURNS

In the not too distant past, most patients with moderately severe third degree burns were doomed to a stay of many months in a hospital, with the certainty of disfiguring scars, serious crippling and loss of function of the involved parts, permanent deterioration in general health, and often a lifetime of invalidism. Perhaps the greatest advance made during World War II in this field was the dissemination among the thousands of physicians serving in the Armed Forces of already accumulated knowledge concerning the pathologic anatomy, physiology, and proper treatment of burns. The use of explosives and of petroleum products in such large quantities by so many men was bound to result in the occurrence of many accidents, and there were many thousands of burns sustained and treated during the war years. Although little really new information was added, many reports have appeared amply confirming the work of prewar years, the clinical establishment of which might otherwise have required a much longer time.

The management of burned patients has been established on a relatively simple basis following correlation of many recent studies. While the care of burns is much simpler and more effective now than in the days when tanning agents were used, close attention to every detail is necessary.

#### Pathology

Thermal burns are divided ordinarily into three types, according to depth of burn and degree of necrosis.

*First degree burns* are mild, showing nothing more than erythema and slight edema of the involved area, sometimes with later desquamation of the superficial layers of the skin, as in sunburn. The *second degree burn* is more severe, with partial destruction of the skin. Necrosis extends to the deeper layers, although viable epithelium is left behind from which the skin is restored in a few days without residual scarring or deformity. In the more superficial second degree burns, large blebs and blisters develop

almost immediately in the injured area, but healing is rapid and is complete in several days. Deeper second degree burns may involve almost the entire thickness of the skin, spontaneous epithelization occurring a little more slowly from the uninjured remnants of the skin glands and hair follicles. By definition, all types of second degree burns, whether deep or superficial, will heal without need for grafting and will leave little or no scarring. *Third degree burns* are those which destroy all the layers of the skin as well as all the deeper epithelial elements from which spontaneous skin replacement might occur. Spontaneous healing of third degree burns can occur only by growth of epithelium inward from the margins of the wound and shrinkage of the defect, a process which takes months at best and may never occur. Burns of this type require skin grafting almost without exception. *Intermediate* or mixed second and third degree burns are not uncommon. In such burns, epithelial growth develops slowly from the few remaining islands of epithelium deep below the necrotic skin, and the burned surface is finally covered by a thin fragile layer of "scar epithelium" which has little resistance to trauma and usually requires later plastic replacement. The depth of a moderately severe burn cannot always be estimated accurately until healing has begun and demarcation of slough has occurred.

The skin and subcutaneous tissue destroyed by a deep burn form a thick hard slough, densely adherent to the underlying viable tissues. As absorption and repair take place beneath the eschar, it loosens gradually and separates spontaneously after from four to six weeks, revealing a smooth granulating surface. The eschar resulting from a deep burn remains attached longer than the slough caused by a shallow third degree burn in which less fibrous tissue is involved.

*Pain* is most constant and severe in first and second degree burns and is probably due both to irritation of the sensory nerve endings and to capillary congestion beneath the injured area. Patients with severe and extensive burns may show surprisingly little pain, probably because the superficial nerve endings are destroyed with the skin.

Local trauma due to a burn, like trauma due to any other injurious agent, produces a proportionate degree of underlying inflammation. Capillary congestion may be the only result of a first degree burn, while more severe injury is followed by exuda-

tion of fluid from the capillaries and accumulation of fluid in the adjacent tissues. If the burn is relatively superficial, the fluid exudate produces blebs beneath the destroyed epithelial layers; if the burn is deep, the tissues become swollen with the plasma-like capillary filtrate. The blister fluid, probably identical with the fluid accumulating in the subcutaneous tissue, contains a large amount of protein, chiefly serum albumin, and resembles blood plasma in composition except for its low content of globulin. Very large quantities of fluid, amounting in some cases to more than half the total plasma volume, may be lost into the tissues according to the depth and extent of the burn. Continued exudation of fluid into the burned area results in a progressive loss of fluid and protein from the blood stream, even though much of the fluid is reabsorbed by the lymphatics.

A mixed burn or even a deep second degree burn may be converted into a third degree burn if the surface becomes infected. Although the undisturbed fresh burn surface is by no means sterile, bacteria on the surface do not ordinarily gain entry through the coagulated and cooked eschar as long as it remains intact, no matter how thin or how thick it may be. Bleb fluid is usually sterile, but if the blisters are opened and the raw surface handled carelessly or roughly, microorganisms may be carried below the protective coating to the deeper layers. Infection or trauma may destroy the islands of epithelium from which skin regeneration occurs, so that the entire future course of a burned patient is largely determined at the time of the first dressing.

*Healing* of a burn follows the pattern of healing of other injuries. As the inflammatory response recedes, the edema regresses and the pain subsides. The necrotic superficial layers separate at the junction between the living and dead cells, and the slough drops off spontaneously. This process is complete after three or four days in superficial second degree burns but may require one to two weeks in deep second degree burns. Epithelial repair in an erythematous burn consists of nothing more than replacement of the outermost layers of cells desquamated following the injury. When the destruction is deeper, the surface becomes covered with new epithelium growing from the viable islands left in the undestroyed skin glands and hair follicles. Separation of the slough covering a third degree burn may require weeks. The absorption and lysis of the connective tissue strands binding



the *slough* to the subcutaneous tissues is a slow process, and a significant amount of scar tissue develops beneath the separating slough. Epithelization of this type of burn is slow and uncertain, occurring by ingrowth of thin epithelial sheets from the margins of the wound. Even if the burn is eventually covered in this way, the healed skin is fragile and unsatisfactory and breaks down frequently.

**Blood Changes.**—The first and most striking changes noted in the blood are the effects of the loss of plasma fluid. Capillary dilatation and plasma exudation in the burned area may result in the withdrawal of large quantities of fluid from the vascular system, sometimes amounting to more than half the total plasma volume. Proportionate degrees of hemoconcentration develop, the hematocrit reading rising from a normal value of 45 to as much as 70 or 75 in extensive burns. Profound alterations in the blood characteristics often occur within two or three hours after the burn is sustained, blood viscosity rising proportionately with the hematocrit, and the red cell and white cell counts exhibiting similar degrees of increase. Later, as lymphatic reabsorption of the accumulated fluid occurs, the spontaneous restoration of fluid decreases the rate of plasma loss and the hematocrit begins to decline toward normal. After several days, when the blood volume is approaching an approximately normal value, anemia appears. It is probable that a significant degree of red blood cell destruction occurs in the region of the burn at the time of injury, for hemoglobinemia and hemoglobinuria are present to some degree in all severe burns. Hemolysis is masked by hemoconcentration during the early stages, and its effects are seen only after the normal blood volume has been restored.

**Visceral Changes.**—Liver damage as a result of burns is not usually of great importance. The hepatic focal necrosis and impairment of hepatic function reported in the past probably were results of the current methods of treatment rather than of the burn itself. The tannic acid treatment and its variations have been almost universally abandoned since the demonstration of the absorption of tannic acid through the burned surface and of its hepatotoxic effect.

Renal damage, however, does occur following burns and usually is proportionate in degree to the severity of the burn.

Several causative factors are involved in the kidney damage, particularly secondary shock, diminution of renal blood flow, and hemoglobinuria. Examination of the damaged kidney at necropsy reveals that most of the visible pathologic change is in the tubules,<sup>1</sup> which show cellular necrosis and contain pigmented casts. Clinical evidence of renal damage in patients with burns of more than moderate severity includes oliguria, albuminuria, casts in the urine, and elevation of blood nonprotein nitrogen.

Other visceral changes are less constant and less characteristic. Rarely, acute ulceration of the stomach or duodenum may develop as a complication of severe burns (Curling's ulcer), and focal necroses have been found in the adrenal cortex in patients who have died following extensive burns.

Besides the early hemoconcentration resulting from plasma loss and the subsequent anemia due to red blood cell destruction, other characteristic changes are noted in the body fluids. There is a rapid and well-marked decrease in the plasma chlorides as well as in the plasma sodium because of loss of sodium chloride into the burned area. The blood nonprotein nitrogen is consistently elevated, perhaps as a result of several causes such as impaired renal excretion, increased metabolism (deamination) of protein, and absorption of damaged tissue protein from the area of the burn. The high nonprotein nitrogen level in the blood is accompanied by the excretion of unusually large quantities of nitrogen (urea) in the urine, a loss which continues for several weeks after the original injury. Body protein is lost not only in this manner but also as exudate from the burned surface, either as a clear plasma-like drainage or as a purulent exudate.

The loss of large quantities of nitrogen results in rapid loss of weight and profound wasting of body tissues, both characteristic of burned patients. Because of the severe depression, both psychologic and physical, these patients find it difficult to take food, and the protein loss and malnutrition become progressive.

**Early Complications.**—The pathologic physiology of serious burns is particularly likely to result in *shock*. The sudden severe pain and the intense psychic stimulation result in neurogenic or primary shock, which is transitory and responds satisfactorily to the proper drugs and reassurance. Secondary shock, however, may appear several hours later and is a serious complication. Its occurrence is not always predictable; in some patients,

relatively extensive burns may cause little physiologic disturbance, while in others profound depression or shock may result from apparently minor burns.

Burn shock, formerly the chief cause of death from burns, is now more controllable since the advent of stored blood and plasma. Like other types of secondary shock, the shock following severe burns is due chiefly to rapid and continued loss of fluid from the vascular system. Profuse seepage of protein-containing fluid takes place through the injured capillaries in the region of the burn, with consequent reduction of total and of circulating blood volume, drop in blood pressure, and decrease in cardiac output. Much of this fluid is lost by drainage from the open surface of the burn, although the fluid in the deeper layers is reabsorbed later through the local lymphatics. Hemoconcentration, often of marked degree, develops within a few hours, and the blood viscosity is concomitantly increased, further retarding the velocity of flow through the capillary system. It is also believed by many investigators that toxic substances are produced by the tissue injury in the burned area and play a part in the production of shock. Although toxins may contribute to the development of burn shock, it is probable that the rapid loss of fluid from the vascular system is sufficient in itself to account for the circulatory collapse.

As in shock due to any severe injury, visceral function is impaired in burn shock. Oliguria develops rapidly and the kidneys may suffer serious damage and even permanent impairment of function from the depressed renal circulation. Liver function is depressed, and the normal absorptive and peristaltic activities of the gastrointestinal tract cease until the blood volume and blood pressure can be elevated above shock level. Pneumonia may appear because of the generally decreased resistance to infection, particularly in those patients who have inhaled smoke or hot gases.

The extensive open surface of a burn renders it particularly liable to the development of *infection*. The tissue defenses are well able to cope with the bacteria remaining on the burned surface following the injury, and infection rarely arises from such organisms. Most burn infections result from secondary contamination by improper first-aid measures, by unsterile instruments or dressings, by droplets sprayed from the nose or mouth

of an unmasked attendant during the dressing of a burn, or from surface bacteria given an excellent chance to grow following excessive traumatization of the burn surface by a rough first dressing or a too early second dressing. While the slough covering a deep burn may contain bacteria, it usually protects the underlying surface from the development of clinical infection; after separation of the slough, bacteria are almost uniformly present on the granulating surface, as in any granulating wound.

### Treatment

Evolution of the present methods of treatment of burns has kept pace with the progress in elucidation of the pathologic physiology involved. Proper management of the severely burned patient demands almost simultaneous treatment of every phase, and every manifestation of the injury, both local and systemic, according to a previously worked-out and definitely planned procedure. To combat shock, blood and plasma transfusions are given and morphine may be administered while treatment of the local injury is progressing. Possible complications, such as shock, anemia, pneumonia, infection, destruction of the skin, scarring, malnutrition, loss of weight and strength, and mental depression, must be foreseen and every possible precaution taken to prevent or at least to minimize their development. Although the pain, shock, and local damage must all be treated promptly and at the same time, the therapeutic procedures applicable to each will be discussed separately.

**Treatment of the Burn.**—The introduction of the *tannic acid* treatment was a great step forward in the application of physiologic principles to the treatment of burns. The coagulum formed on the burn surface by tannic acid decreased the loss of fluid, acted as a protective dressing, and diminished the severe pain. Tannic acid has now been abandoned almost entirely for several reasons. The fixing or precipitation of surface proteins by tannic acid is not limited to tissues already destroyed but involves the upper layer of viable cells on the exposed area. Deep second degree or mixed second and third degree burns consequently are transformed uniformly into third degree burns, so that most of the tanned surface is likely to require skin grafting. Infection frequently develops under the eschar from bacteria

already present when tanning is begun. The resulting purulent exudate is imprisoned beneath the coagulum, with widespread destruction of fragile regenerating epithelium and viable epithelial remnants. Finally, tannic acid is absorbed to some degree through the raw surface and produces focal necrosis in the liver,<sup>2</sup> occasionally with fatal results.

Other methods of surface coagulation or tanning, such as application of tannic acid together with silver nitrate, or spraying of the burned surface with gentian violet or triple dye are subject in a lesser degree to the same disadvantages as tannic acid. Use of tanning agents in treatment of burns has decreased generally because of these disadvantages.

Cannon and Cope<sup>3</sup> demonstrated by clinical experiments that tanning agents not only delay epithelization but sometimes even prevent it. Donor areas from which split-skin grafts had just been taken were treated by one of the various techniques used for dressing fresh burns, until the effects of each of the methods advocated for burn treatment had been investigated in a satisfactory series of experiments. The results demonstrated that tanning agents not only prolong the time ordinarily required for healing, but also sometimes so damage the surface that skin grafting becomes necessary. Of all the agents tested, tannic acid caused the greatest retardation of healing and the most widespread damage to the regenerating epithelium. The most consistently rapid and complete healing was obtained by the use of boric acid gauze pressure dressings.

Current methods of local treatment differ in details but in general are based upon *minimal cleansing or débridement* of the burned surface and application of a layer of fine-meshed gauze next to the burn, with or without the use of a bland oil or grease to prevent adherence, with a fairly bulky, moderately snug outer *pressure dressing*, not to be changed for at least ten to fourteen days. This type of dressing has been advocated since 1937 by Allen and Koch,<sup>4</sup> who maintain that a burn is a special type of large open wound and should be treated as such. These authors have also advocated thorough but gentle cleaning and débridement of the entire burn surface.

Complete aseptic surgical technique is mandatory for the first and for all subsequent dressings of a burn, just as it is for the treatment of an extensive traumatic wound. If at all possible,

all burn dressings should be changed in the operating room rather than on the ward until all involved surfaces are covered with viable epithelium.

It is unnecessary either to wash or to débride the burned surface, even if simple home remedies were applied before admission. The bacteria contaminating the surface cannot all be washed away and the ones below the surface cannot be reached. Similarly, it is impossible to remove all the necrotic tissue; in many cases one cannot even tell whether the recently sustained burn is second or third degree in depth. Many surgeons, however, prefer to wash the burn gently but thoroughly with white soap and sterile water and to remove all visibly destroyed epithelium with sterile instruments. This method is subject to the disadvantages that it consumes time unnecessarily, causes pain, and increases fluid loss; it may even promote the subsequent development of infection by removing the protecting surface layer of coagulated exudate. It is possible also that the trauma of cleansing and débridement, however gentle, may destroy viable bits of epithelium still remaining on the burned surface, thereby preventing or delaying spontaneous healing. Gross surface dirt should be washed away by gentle irrigation with normal salt solution, and it is justifiable to open large tense bullae that would cause pain beneath a pressure dressing and to clip away the overlying skin. Any further manipulation of the burned surface should be reduced to a minimum.

Morphine is given as indicated (p. 532) but no general anesthesia should be used for the primary dressing. If the treatment of the burned surface causes pain, it probably is being done too vigorously. If application of the pressure dressing causes pain, it probably is being wound too tightly or over too little or too dense padding.

*Fine-meshed gauze* (44 mesh) is applied to cover the entire burn, avoiding any wrinkling or crumpling. The gauze may be prepared beforehand by cutting three-inch wide gauze roller bandage (44 mesh) into six-inch lengths, placing them in a flat pile in a suitable container, and sterilizing. The gauze may be applied dry or moistened with sterile normal salt solution, or it may be impregnated with petrolatum or boric acid ointment and sterilized before use. There is little difference in subsequent healing no matter which type of gauze is employed as a dressing, but it must



Fig. 57.—Pressure dressing for burns. Sterile petrolatum gauze is applied aseptically. Neither the burned area nor the inner dressings are touched with the fingers, even though gloved. In burns of the hand, each finger is dressed separately.



Fig. 58.—Pressure dressing. Flat gauze sponges are applied smoothly over the grease gauze.



Fig. 59.—Pressure dressing. Sterile waste or fluffed gauze is applied over the flat sponges. It is fixed loosely with a few turns of gauze bandage.



Fig. 60 — Pressure dressing. Application of elastic bandage. The bandage is applied snugly but not tightly. When such a bandage is applied to the hand, the hand and fingers should be in the position of function: wrist slightly extended, fingers slightly flexed and separated, and thumb in mid-abduction and slight flexion.



be fine meshed. If ordinary coarse gauze sponges are used, the meshes are pressed into the burn and become adherent to it, so that epithelization is impeded and the formation of granulation tissue is encouraged. If not previously prepared, fine-meshed gauze strips may be cut as needed from a sterile roller bandage. Other nonadhering dressings which may be used, according to personal preference, include silk, soft linen, rayon, and fine-meshed nylon gauze (Figs. 57, 58, 59, 60).

The next layer of the dressing consists of one or two thicknesses of flat gauze sponges, followed by enough sterile mechanics' waste or fluffed gauze to make a layer at least one inch thick when finally compressed. The dressing is held in place by a thick gauze or cotton roll, and elastic compression is applied by a woven elastic bandage applied snugly but not so tightly as to cause pain. The dressing should extend four to six inches beyond the burn if possible.

**Burns of the Extremities.**—If the burn is extensive, the hand or foot should be incorporated in the dressing even if uninjured. Otherwise interference with venous return and edema of the extremity may develop following application of a tight compression dressing proximally. Burned fingers or toes must be dressed separately so that the denuded surfaces of adjacent digits cannot come in contact with each other, lest they granulate together. When the hand is dressed, the fingers are slightly flexed at all joints, the thumb is slightly abducted, and the wrist placed in very slight extension (position of function). The burned foot is held at a right angle and in slight inversion in the dressing. Other joints are maintained in slight flexion rather than full extension. Some authorities advise the use of a molded plaster splint to prevent excessive motion, but splinting is not necessary if a sufficiently voluminous dressing is applied.

Fixation in close-fitting plaster casts has been suggested for burns of the extremities but is not yet widely used. In this type of dressing,<sup>3</sup> fine-meshed gauze is applied to the burned surface, followed by four layers of sterile open gauze sponges applied without wrinkling or overlapping. The dressing is completed by the application and careful molding of thin anterior and posterior plaster splints, covered when beginning to set by a thin layer of

circular plaster bandage. The cast covers the entire distal extremity and extends several inches proximal to the burn. The chief disadvantage of the plaster dressing is that localized pressure necrosis may occur beneath the cast.

**Burns of Other Areas.**—Pressure dressings cannot be applied to the chest, abdomen, or back without interfering with respiration or causing constant discomfort. Burns of the trunk therefore are treated by application of a bulky dressing fixed with adhesive tape, without the elastic bandage.

Burns of the face are treated with a compression bandage covering the entire face and head, with small but sufficient apertures left for the nose and mouth. If the eyes or eyelids are burned, gentle irrigation is performed with sterile normal salt solution, a little sterile petrolatum is applied, and the eyes are closed and are also incorporated in the pressure dressing. A small pad of fine-meshed gauze is placed behind the ears before application of the dressing. Pressure dressings on the face can be removed after seven days, for the skin of the face heals somewhat more quickly than that elsewhere on the body. Lund and associates<sup>6</sup> have given up the use of pressure dressings in treatment of burns of the face, head, and neck, feeling that sufficient pressure cannot be applied and that the dressing is too uncomfortable. These authors prefer the use of sterile petrolatum gauze strips applied with no other dressing or cover and replaced with similar strips by the ward nurse as they become disarranged. Both methods yield good results and may be used as the circumstances warrant.

It is almost impossible to apply a pressure dressing to the perineum and genitalia. Burns of these areas are covered with strips of sterile petrolatum gauze, changed as necessary. Extensive third degree burns involving the perineum and anus may require sidetracking of the fecal current by temporary colostomy until complete healing is attained. With less severe burns, the patient should be constipated for a week by a low-residue diet and appropriate dosage of paregoric or of lead and opium pills; after this time, an enema is given.

**General Treatment.**—Upon entrance to the hospital, the patient is examined for evidences of shock, and the extent and severity of the burn are determined. Clothing is removed

gently; any portion adherent to the burned surface is soaked with sterile normal salt solution and detached after it has loosened. Exposed burned surfaces are covered temporarily with a sterile sheet and the patient is covered with a blanket. A specimen of blood is secured for hematocrit and blood count determinations. Tetanus antitoxin or toxoid (p. 538) is administered in every case. Sedatives are not needed as a rule, although narcotics are given as required for control of pain or excitement.

*Morphine*, when administered to patients in actual or threatened shock, is best given in a dose of 8 to 16 mg. (gr. 1/8 to 1/4) intravenously, repeated after a half hour if necessary. Patients in shock show delayed absorption; morphine given subcutaneously may produce no effect for several hours, by which time the patient may have had several large hypodermic doses. Following subsequent elevation of blood pressure by administration of blood and plasma transfusion, improved absorption may result in the development of morphine poisoning. This effect was noted also by Beecher<sup>7</sup> in battle casualties recovering from shock.

Patients with minor burns are able to take the required amounts of fluids and food orally and transfusions and infusions may be unnecessary. The severely burned patient, however, requires *rapid restoration of fluid* to replace the plasma that is being steadily drained from his vascular system. Only a few hours are required for loss of an amount of plasma sufficient to produce clinical shock, and administration of plasma must keep pace with its loss during the period of approximately forty-eight hours that this loss continues. The amount and rate of loss of the plasma that filters out of the vascular system into the burned area depends upon the extent of the burn as well as upon the depth, so that an extensive second degree burn may be more immediately dangerous than a less extensive third degree one. The quantity of plasma required for replacement can be estimated roughly at first by the percentage of body surface burned and later by the degree of hemoconcentration and the quantity of urine excreted.

A burn of 10 per cent of the body surface is incapacitating and may require transfusion of blood or plasma for replacement of the vascular fluid loss. More extensive burns are proportionately more dangerous, and a severe burn involving 20 per cent or more of the body is likely to prove rapidly fatal unless shock is forestalled

by immediate and adequate replacement therapy. Because most of the fluid loss occurs within the first few hours and declines in rate during the next twenty-four to thirty-six hours, prompt transfusion is necessary. If *plasma* is used rather than whole blood, the amount required can be determined approximately in different ways. Harkins<sup>8</sup> has suggested the administration of 50 c.c. of plasma for each 1 per cent of the body surface burned, the total amount of the plasma required to be given within twelve hours after injury. Estimation of body surface involved may be made according to the measurements determined by Berkow<sup>9</sup>

REGION	PER CENT OF BODY SURFACE
Head and neck	6.0
Upper extremities	
Both arms and forearms	13.5
Both hands	4.5
Total	18.0
Trunk	
Anterior surface	20.0
Posterior surface	18.0
Total	38.0
Lower extremities	
Both thighs	19.0
Both legs	12.7
Both feet	6.3
Total	38.0

These measurements were repeated more recently by Lund and Browder,<sup>10</sup> who agree fairly closely with the percentages for adults but find more difference in percentages between adults and children of varying ages than Berkow had noted. Charts with body diagrams and area percentages according to their findings were described by these authors and suggested for use as clinical records for burn cases.

If laboratory facilities are available, hematocrit determinations may provide additional and more dependable information for estimation of plasma transfusion requirements. Harkins<sup>8</sup> has suggested also the administration of 100 c.c. of plasma for each 1 per cent rise above the average normal value of 45 in the hematocrit. Jenkins and associates have devised a nomogram (p. 148)

to indicate the amount of plasma or blood required according to variations in the hematocrit. These dosages are decreased proportionately in children according to age and weight. Both authors stress the fact that repeated hematocrit determinations at frequent intervals are necessary to keep pace with the changes in the blood volume and in the ratio of cells to plasma as the plasma loss continues. The need for supplementary transfusions and the minimum amounts required are determined by clinical response and by frequent blood examination; the fluid requirement calculated from the initial hematocrit reading covers only the amount lost up to that time and does not provide for subsequent continuing losses.

Administration of plasma is begun as quickly as possible if the burn involves 15 per cent or more of the body surface. The initial dosage required is calculated according to surface extent of the burn or degree of hemoconcentration; half of this amount is given within the first three to four hours and the entire amount within the first twelve hours. Proper replacement therapy may require transfusion of as much as 3 to 4 liters of plasma each day for two days before oliguria and hemoconcentration disappear. If the superficial veins temporarily become too severely damaged for use, the external jugular, saphenous, and femoral veins can be used.

Cope and Moore<sup>17</sup> have suggested the following formula for fluid therapy during the first forty-eight hours for patients with burns of more than 30 per cent of the body surface:

1. For wound edema, a volume equal to 10 per cent of the body weight.
2. For external loss an amount varying according to the area of wound surface:

Burns of 25-35 per cent	= 1,000 c.c.
35-60 per cent	= 2,000 c.c.
60 per cent and over	= 3,000 c.c.

Of the total, two-thirds is given as plasma and one-third as isotonic electrolyte solution. One-half is given in the first twelve hours, one-fourth in the second twelve hours, and the remaining one-fourth in the next twenty-four hours (calculated from the time of the burn rather than from the time of admission). In addition, 1,500 c.c. is given each day for renal excretion, one-half

as isotonic electrolyte solution intravenously. Finally, 1,500 c.c. of water or dextrose solution is given daily for insensible fluid loss. The state of balance between fluid needs and supply, according to this plan, can be followed by insertion of a retention bladder catheter and hourly observation of urinary output, which should average from 50 to 200 c.c. each hour.

During the first day the blood pressure is taken and recorded every half hour. Hemoglobin or hematocrit determinations are made every two hours until normal values are reached and maintained. Falling or subnormal systolic pressure or rising hemoglobin or hematocrit values indicate the need for further transfusion.

In the experience of many observers in the medical department of the Armed Forces during World War II, it was found that the use of *whole blood* is not only uniformly necessary after the fourth or fifth day following a burn, when secondary anemia becomes apparent, but is also of considerable value as immediate treatment in preventing shock.

Several factors are involved in the rationale of the use of blood rather than plasma during the first two days. While the hemoconcentration secondary to burns indicates loss of plasma and depression of the total as well as the circulating blood volume, it is not necessarily true that equal replacement of the lost plasma will restore the blood volume and hematocrit to normal. Loss or destruction of red blood cells as well as transudation of plasma occurs during and after a burn; the blood volume therefore is decreased with respect to erythrocytes as well as to plasma. A deficit in blood volume proportionate to the loss of red cells still remains even after enough plasma is administered to restore the hematocrit and cell count readings to normal. Introduction of enough plasma to replace the plasma loss fully will, in many instances, produce hemodilution, which is especially likely to appear after the third or fourth day when absorption of the fluid exudate in the area of the burn takes place.

Blood loss<sup>11</sup> at the time of the burn probably is due to increased fragility of the red cells which were subjected to the thermal trauma; hemolysis occurs, with hemoglobinuria. Blood loss during the following weeks probably is due to the widespread infection of the burned surface as well as to inhibition of red cell regeneration.

For these reasons, transfusions of blood as well as of plasma are indicated in the acute stage of the burn, even though elevation of the hematocrit is noted. The transfused erythrocytes remain in the vascular channels and increase the power of the blood to retain fluid as well as to carry oxygen to the viscera and prevent shock. Plasma transfused alone increases the blood volume temporarily but is soon lost to a great extent through the highly permeable capillaries in the burn areas. It is too soon to say positively whether plasma transfusions should be replaced entirely by whole blood in the early treatment of burns; it is probable that a varying proportion of each fluid will be most effective, depending upon the degree and the extent of the burn, the tendency to shock, and the hematocrit values. In severe burns, certainly a large portion of the fluid transfused during the first two days should be whole blood.

A clinical study of the use of blood rather than plasma has been reported by Evans and Bigger.<sup>12</sup> These investigators found by blood volume studies that in severely burned patients the red cell deficit averaged 40 per cent of the total volume deficit. A series of thirty-two seriously burned patients were treated with pressure dressings, whole blood transfusions of 500 to 1,000 c.c. every six hours for the first two days, and sufficient fluids to keep urinary output at an average of 50 to 100 c.c. per hour. No plasma was used. Fluids were given orally by preference, in any form the patient preferred, and no effort was made to increase the salt intake. Sodium bicarbonate was given in doses of 8 Gm. for each transfusion. For children under 5 years of age, transfusions of 150 to 200 c.c. of whole blood were given every six hours, and in all patients enough blood was given to maintain the hemoglobin level above 100 per cent during the first four days. Penicillin was used. While the authors make no final statements as to superiority of whole blood transfusion over plasma in the early treatment of burns, they believe that the use of whole blood prevents development of secondary anemia, maintains the plasma proteins at more nearly optimum levels, keeps the urinary output high, and tends to promote more rapid epithelization of the damaged surface.

Abbott and associates<sup>13</sup> also advocate the use of whole blood rather than plasma, together with fluids by mouth, in the immediate treatment of burns. Estimation of the quantity of blood

needed is made according to the formula of Harkins (50 c.c. of blood for each 1 per cent of body surface burned) for adults, or in dosage of from 1 to 5 per cent of the patient's body weight in kilograms. The fluid supplied orally during the first forty-eight hours is hypotonic salt solution (two-thirds to three-quarters normal strength) in amounts totaling 10 to 15 per cent of the patient's body weight. These observers state that early administration of whole blood transfusions and oral fluids will combat shock effectively and alleviate the secondary anemia characteristic of the early period of convalescence. They feel that while the hematocrit is not a reliable guide to the proper form of fluid therapy in burned patients, it is probably preferable to use whole blood only if the hematocrit is below 60 and plasma alone if hemoconcentration is more marked.

The use of *adrenal cortical extract* or of desoxycorticosterone acetate has proved of little constant value and is no longer advised in the treatment of burns or of shock.

The *temperature* and *respiration* are noted every two hours while the patient is seriously ill; hyperpyrexia may be treated by cold baths or alcohol rubs on the unburned surfaces at frequent intervals. It is never permissible to use heat tents over recently burned patients; tents are useful to prevent pressure from the bedclothes, but light bulbs are contraindicated.

Inhalation of smoke or of hot air may cause severe tracheitis, bronchitis, pulmonary edema, or pneumonitis. The chest must be examined at intervals during the first few days in all burned patients and the findings recorded. *Oxygen by inhalation* or by means of an oxygen tent is indicated when respirations are labored, and occasionally tracheotomy may be necessary if laryngeal edema develops. The penicillin administered routinely to burned patients helps also to diminish the incidence of pneumonia.

*Fluid output and intake charts* are kept carefully for at least ten days, and enough fluid is supplied to keep the urinary output at its optimum level of 1,500 c.c. daily. Oral administration of fluids is to be preferred; probably a greater percentage of fluid is retained for a longer time if it is absorbed slowly through the gastrointestinal tract than if it is given directly into a vein. The patient may be given almost any type of fluid he desires, and most burned patients will drink fluids willingly. In most patients



with minor burns, fluid balance can be maintained satisfactorily by oral administration of fluids. Infusions are necessary as a rule during the first two days, if the patient is agitated, toxic, or in shock. Most of the fluid given intravenously should be supplied as 5 to 10 per cent dextrose, with not over 2 liters of normal salt solution being given each day unless blood chloride determinations show the presence of hypochloremia. After the third day resorption of tissue fluid occurs at a greater rate than transudation, so that the blood volume may increase spontaneously, with a concomitant rise in plasma chlorides. For this reason, determinations of the plasma chlorides and proteins and of the degree of hemoconcentration are made during the third and fourth days also, even though the danger of shock is past. Excessive administration of fluids during this period may cause pulmonary edema and tissue edema, particularly if any kidney damage has developed.

*Prophylaxis of infection* is necessary, since infection is a frequent complication, delaying healing, prolonging convalescence, increasing deformity, and often converting a mild burn into a severe one. Immediately after injury the burned surface is only slightly contaminated, if at all, by bacteria, but microorganisms are quickly inoculated onto the wound by air currents, application of unsterile material or dressings, and particularly by droplets from the nose and mouth of any unmasked attendant. Rough or prolonged handling or cleaning of the burn may initiate infection.

Such infection is rarely due to a single organism, the exudate showing many different forms. Staphylococci, both hemolytic and nonhemolytic, streptococci of various types, *Proteus vulgaris*, *Escherichia coli*, and *Pseudomonas aeruginosa* are the most common offenders. *Clostridium tetani* is present occasionally, and administration of tetanus antitoxin (1,500 to 3,000 units) is advisable both immediately and at the time of débridement of the slough. If the patient has been immunized previously, a "booster dose" of tetanus toxoid (1.0 c.c.) is preferable.

Eradication of infection from a burned surface is extremely difficult; avoidance of contamination is much simpler and safer. Minimal cleansing and minimal manipulation of the burn during dressing, use of the same aseptic technique used in a clean surgical operation both at the first treatment and at each sub-

sequent dressing, and close watch on the wards to make sure that the dressing remains sealed over the burned area are all necessary. When the burn is exposed during dressing, all personnel in the room must be fully masked; even the patient should have at least a towel across his nose and mouth. Dressings are done as infrequently as possible; the first dressing is not changed for at least ten days, and reparative grafting usually can be done after not more than one or two other dressings (p. 541).

The prophylactic systemic administration of penicillin and of sulfadiazine is of established value in the care of burns. Penicillin, which is most effective against staphylococci, is given subcutaneously in doses of 25,000 units every three hours for the first five or six days, after which it can be discontinued with safety. For two days before and three days after application of skin grafts, the prophylactic systemic administration of penicillin is also indicated. Sulfadiazine, which is particularly effective in depressing the growth of streptococci, is given in full therapeutic dosage, with double dosage of sodium bicarbonate, for the first week. The two drugs may be given simultaneously.

Langohr and associates<sup>14</sup> have made a detailed study of the bacteriology of burn wounds. According to their findings, staphylococci can be restrained by use of penicillin for perhaps three weeks, although the growth of gram-negative organisms is correspondingly increased during this time. Some of the strains of staphylococci present, including the types of high virulence, will develop resistance to penicillin after several weeks so that by the fifth week the burn surface is a quagmire of penicillin-resistant and penicillin-inhibiting organisms over which the drug exerts little control. These authors point out that the quickest way to starve the bacteria is by early surgical excision of the burn slough, which also accomplishes their removal. If the slough is not excised promptly, treatment with penicillin, sulfadiazine, and even streptomycin, together with administration of tetanus and gas gangrene antisera, may be advisable.

The local use of drugs on the burned surface has not proved of value. Penicillin is absorbed too rapidly; unless it can be combined with a bland nonirritating grease or ointment from which it will be released slowly, its effect is too transient. Sulfonamides applied locally appear to be irritating to the burn. Furthermore, soluble sulfonamides such as sulfanilamide are absorbed within a

few hours from the open surface of the burn. A transient high level of sulfanilamide in the blood results, with a rapid subsequent decrease. After absorption through the burn surface, sulfonamides applied locally obviously can produce no further bacteriostatic effect on the surface of the burn. Systemic administration, therefore, is much more effective in prevention of invasive infection. Insoluble sulfonamides such as sulfathiazole and sulfadiazine are ineffective therapeutically when undissolved and may produce local irritation and damage by acting as foreign bodies. The incorporation of irrigating tubes in the dressing, leading to the burn surface from the outside for administration of antibacterial solutions, is more likely to result in the introduction of additional bacteria than in the destruction of those already present. For these reasons no local application of any medication other than sterile petrolatum to the burn surface is advised.

**Secondary Dressings.**—Dressings are not changed before at least ten days have passed. If the patient complains of pressure or of severe itching or if the dressing becomes odorous, the outermost layers may be changed or additional clean gauze may be applied. The deeper half of the dressing must not be disturbed unless the patient develops constant localized pain suggestive of infection, with elevation of temperature.

At the proper time, the dressing is changed in the operating room under aseptic conditions. The deep layers of gauze are almost always stiff with dried exudate and are adherent to the skin. Warmed sterile normal salt solution, applied with a bulb syringe, is used to soften the deeper dressings after the outer layers have been removed. Anesthesia is not usually necessary; if the gauze is properly moistened and is removed gently and slowly, little pain will be produced even on open third degree areas. Dressings must never be pulled off quickly, under the mistaken impression that sudden removal causes less pain, as in the case of adhesive tape. Rough handling is almost certain to cause destruction and tearing of fragile new epithelium and of smooth surface granulations, with resulting loss of skin and danger of infection, delayed healing, and increased scarring. By ten days after injury, second degree burns will be covered completely with new epithelial layers, and mixed second and third degree burns will show advanced healing. If it appears likely that epitheliza-

tion is still progressing, a second dressing exactly like the original one is applied. No further local treatment is done at this time. The plan of treatment should be explained to the patient and his family, who otherwise are likely to be disturbed at the apparent neglect in delaying change of dressings

**Skin Grafting.**—After a second period of ten days has passed, the dressing is again changed in the operating room, with the patient prepared for anesthesia if necessary. By this time maximum spontaneous healing has occurred and any areas remaining unhealed or still covered by slough will require grafting.

Small third degree burns will often heal by ingrowth of epithelium from the edges, and larger burns of mixed degree may heal slowly by epithelial outgrowth from a few small remnants of skin glands. In both cases the epithelium is likely to be composed of a thin layer of epithelium over a scar tissue base, with little resistance to trauma and a tendency to frequent ulceration. Such areas ("scar epithelium") are best treated by excision of the defective skin and replacement by a split-skin graft from a healthy area. While skin of the scar type is not permanently satisfactory, it will serve as a temporary covering until other more deeply burned areas have been grafted.

By this time all second degree burns are well healed and mixed burns have a satisfactory covering. Areas of third degree burn are either granulating or are covered by a thick slough. If no infection is present, preparation for grafting of such areas may be done at this time.

**PROCEDURE.**—For burns of the extremity, a loose tourniquet is applied proximally well above the burn and general anesthesia is induced by administration of either sodium pentothal or cyclopropane. The burned area is cleaned by irrigation with sterile normal salt solution and sterile drapes are applied with care. The tourniquet is tightened (or inflated) by an unsterile assistant, and débridement of the third degree burn is performed. All slough is excised, including necrotic fascia, necrotic portions of tendons, and nonviable cartilage. Granulation tissue is removed by rapid excision of the upper layers rather than by scraping. Débridement is continued until all nonviable tissue, including the marginal epithelium, has been

excised and a healthy base remains. The tourniquet is released and pressure is applied by means of dry sponges, with a layer of dry fine-meshed gauze next to the wound. Gentle but adequate pressure is maintained for from three to five minutes, after which time most of the bleeding should have stopped. The use of gelatin sponge or fibrin foam and thrombin solution is not advised; these substances remain on the wound surface and act as foreign bodies. Occasionally, a small artery or a relatively large vein will require ligation or suture with 00000 silk. A pressure dressing is applied, with a layer of fine-meshed gauze next to the wound. The fine gauze may be used dry or moistened with normal salt solution, but no grease is employed at this time. Moderate blood loss may occur during the procedure.

Prophylactic penicillin therapy is begun, and a complete blood count taken. If anemia is still present, it is corrected by whole blood transfusions. After two days have passed, the patient is returned to the operating room, general anesthesia is induced, and the dressing is removed under aseptic precautions. The entire surface should be covered by a very thin smooth layer of healthy granulation tissue, with no evidence of infection and no bits of necrotic tissue remaining.

Grafting of the entire granulating surface with split-thickness grafts is then performed as quickly and as completely as possible. Some degree of skill is necessary in the use of the knife or of the Padgett dermatome if large areas are to be covered. The reasons for the interval of two days between débridement and grafting are (1) assurance that no necrotic tissue has been left behind, (2) assurance of a smooth base of firm fresh granulations for grafting, and (3) avoidance of the danger of bleeding or serous exudation beneath the graft. However, if the surface is granulating cleanly and no necrotic areas are present, it is quite satisfactory to excise the granulations and apply grafts without delay. The only danger of the delay is that one more opportunity for infection of the burn surface is added. No more than two days should be allowed to elapse between débridement and grafting.

The use of "pinch" grafts is decreasing in popularity. Most burn surfaces that will take such grafts satisfactorily can also be cleaned sufficiently to be acceptable for split-skin grafts. Small deep skin grafts produce an unsightly scar, are somewhat un-

satisfactory functionally, and prevent the later use of the surface from which they are taken for split grafts.

Full-thickness grafts can be used to cover small burns of special areas, such as the eyelids. Pedicle grafts or flap grafts are used to correct certain burn deformities but not until after the burned surface has been healed cleanly by means of a split-skin graft.

Skin grafts should be applied only to clean firm smooth red granulations. If the granulations are lumpy, edematous, and pale, the graft probably will be unsuccessful. The surface may be improved by excision of the unhealthy tissue down to a smooth vascular base, with application of a dry, fine-meshed gauze pressure dressing for two days.

Other methods of approach to the grafting of burns are advocated. Many surgeons prefer to delay the first dressing until the fourteenth day and to débride and graft the unhealed areas in one stage at that time. Others prefer to delay both débridement and grafting until still later but to perform both procedures at the same time. A method of management in wide use is to delay application of skin grafts until the slough has separated spontaneously, which may require from four to six weeks. Such delay is subject to the disadvantages that scar tissue formation is increased, opportunities for development of infection are multiplied, and the patient is hospitalized for a longer period; better results are obtained if grafting is done early. Connor and Harvey<sup>16</sup> have had success in prompt removal of even deep burn sloughs by application of pyruvic acid in starch paste (p. 487), which is stated to effect separation of the sloughs within seven to ten days. Cope and associates<sup>16</sup> report good results following excision and immediate skin grafting of third degree burns within the first hours after injury. However, it is often difficult to estimate the depth of a burn at the time of injury; *unless the surgeon has had wide experience in caring for burns*, early excision of the slough may be incomplete and the graft may then fail to grow. Operative trauma at this time also may increase the tendency to development of shock.

Infection of a third degree burn surface is a troublesome complication. Presence of a few bacteria on culture is practically constant for all burns, but production of pus, presence of many microorganisms, and edema of the granulating bed indicate the

necessity for corrective measures. Such infections appear in open third degree burns of more than three weeks' duration. Gram-positive cocci can be restrained temporarily by means of penicillin, administered systemically in therapeutic dosage and locally as wet dressings (1,000 units of penicillin per cubic centimeter of normal salt solution). Infections with *Escherichia coli* and *Proteus vulgaris* respond quickly to treatment with streptomycin applied locally as wet dressings, in concentrations of 1.0 mg. to each 2 to 4 c.c. of solution. If the bacterial growth is widespread, parenteral administration of streptomycin in doses of 0.125 to 0.375 Gm. every three hours may be necessary.

*Pseudomonas aeruginosa* is not uniformly susceptible to treatment with any drug now available. Some improvement can be secured by local application of acetic acid (0.5 to 1.0 per cent) on wet dressings changed twice a day. The use of a dry sterile fine-meshed gauze dressing changed daily under aseptic precautions, however, may produce still better results. The organism grows best in moist surroundings and soon gains some tolerance to acetic acid. Daily dry dressings, although tedious, will keep the wound in better condition and will render the medium less suitable for bacterial growth. Sufficient control of the infection is obtained within five or six days, as a rule, to permit grafting, even though a few organisms may still be demonstrable on culture. If this method is employed, penicillin is given parenterally as prophylaxis against further contamination with coccal organisms.

In general, every satisfactory plan of burn care is based upon prevention of shock, restoration of lost blood and plasma, maintenance of nutrition, provision of optimum conditions for spontaneous repair, prevention of infection, and application of skin grafts to the unhealing surfaces as quickly as possible. Delay in skin grafting results in the development of infection, scarring, and contractures and in loss of function far beyond that originally produced by the burn. In the absence of infection, it is hardly worth while to delay skin grafting beyond three weeks after occurrence of the burn; tissue unhealed by that time will fail to heal later and should be excised before infection develops and causes further damage. The patient is confined to bed for as short a time as possible; he should be encouraged to walk about or to sit up in a wheel chair as soon as his condition will permit.

**Diet.**—The chief nutritional concern is the effective replacement of the large quantities of nitrogen lost both in the region of the burn and in the urine. The rate of loss is most marked during the first three days, although it continues to a high degree during the following weeks. Immediate correction of nitrogen loss is accomplished solely by the administration of plasma and blood transfusions; after the acute stage has passed, the oral and parenteral intake of nitrogenous foods must be made not only to balance but also to exceed the nitrogen loss. Rapid and profound loss of weight and strength and severe wasting of muscle tissue are characteristic of burned patients.

Administration of plasma and blood transfusions is perhaps the simplest means of supplying protein to a patient in negative nitrogen balance. Because of the low protein content (60 to 70 Gm. of protein per liter of plasma) and the slightly deficient quality of plasma protein for general nutritional needs, it is impossible to supply sufficient plasma by transfusion to bring a burned patient into nitrogen equilibrium. If a satisfactory protein intake is not provided, weight loss to the point of emaciation occurs, healing is delayed and regenerated areas may break down, granulation tissue is of poor quality and will not support skin grafts, infection develops and stubbornly resists treatment, and death from cachexia and malnutrition may soon occur.

The diet should supply from three to five times the normal daily requirement of protein, with sufficient carbohydrate and fat to provide at least twice the normal daily caloric intake. In general, the diet is high in protein, carbohydrate, vitamins, and caloric content and relatively low in fat. To be certain that the patient actually receives the prescribed diet, it is best that a definite amount of protein and a definite number of calories be stated. Because the burned patient is likely to be mentally depressed and to have little or no appetite, it is worth while to consult his tastes in food and to have his trays prepared in as inviting a manner as possible. If a relative or special nurse can be present to help him take his meals, his daily intake will be much higher than if he is left to feed himself.

It is difficult to eat so much protein food even if the appetite is normal. Intermediate nourishments high in protein content and in caloric value are invaluable as dietary supplements. Such feedings are usually prepared with skim milk powder, whole



casein, or protein hydrolysate (p. 71). If feedings by mouth remain insufficient, feeding of similar liquid mixtures can be given by stomach tube. Supplementary intravenous injections of protein hydrolysate with dextrose will bring the protein intake up to the quantity desired (p. 76).

The vitamin requirement of the burned patient is far in excess of that of any other type of surgical patient. Because of the role played by vitamins in tissue metabolism, tissue growth and regeneration, and capillary and tissue integrity, large doses of vitamin concentrates or pure vitamin preparations are necessary to insure healing of the burns, successful growth of the grafts, restoration of generally damaged body tissues, and continued normal visceral function. Several times the usual therapeutic doses are given. For example, in severe burns, thiamine chloride (25 mg.), riboflavin (15 mg.), nicotinic acid (100 mg.), and ascorbic acid (500 mg.) may be ordered, each dose to be given twice daily. The dose is kept at this level until healing is well under way and convalescence is advanced, after which the dose is gradually decreased.

Anemia is constant in all burned patients during convalescence. While it is less in degree if the patient has received massive blood transfusions during the early stages, chronic anemia is universally present during recovery and requires treatment by transfusion of whole blood until the normal blood values are approximated. A hematinic drug is prescribed for later use.

### References

1. Goodpastor, W. E., Levenson, S. M., Tagnon, H. J., Lund, C. C., and Taylor, F. H. J.: A Clinical and Pathologic Study of the Kidneys in Patients With Thermal Burns, *Surg., Gynec. & Obst.* 82: 652, 1946.
2. Wells, D. B., Humphrey, H. D., and Coll, J. J.: Relation of Tannic Acid to Liver Necrosis Occurring in Burns, *New England J. Med.* 226: 629, 1942.
3. Cannon, B., and Cope, O.: Rate of Epithelial Regeneration. A Clinical Method of Measurement, and the Effect of Various Agents Recommended in the Treatment of Burns, *Ann. Surg.* 117: 85, 1943.
4. Allen, H. S., and Koch, S. L.: Treatment of Patients With Severe Burns, *Surg., Gynec. & Obst.* 74: 914, 1942.
5. Levenson, S. M., and Lund, C. C.: The Treatment of Burns of the Extremities With Close Fitting Plaster of Paris Casts, *J. A. M. A.* 123: 272, 1943.

6. Lund, C. C., Green, R. W., Taylor, F. H. L., and Levenson, S. M.: Burns; Collective Review, *Internat. Abstr. Surg.* 82: 443, 1946; in *Surg., Gynec. & Obst.* June 1946.
7. Beecher, H. K.: Delayed Morphine Poisoning in Battle Casualties, *J. A. M. A.* 124: 1193, 1944.
8. Harkins, H. N.: Problem of Thermal Burns, *J. A. M. A.* 125: 533, 1944.
9. Berkow, S. G.: A Method of Estimating the Extensiveness of Lesions (Burns and Scalds) Based on Surface Area Proportions, *Arch. Surg.* 8: 138, 1924.
10. Lund, C. C., and Browder, N. C.: Estimation of Areas of Burns, *Surg., Gynec. & Obst.* 79: 352, 1944.
11. Cope, O.: Anemia in Burns (Editorial), *Surg. Gynec. & Obst.* 84: 999, 1947.
12. Evans, E. I., and Bigger, I. A.: The Rationale of Whole Blood Therapy in Severe Burns; a Clinical Study, *Ann. Surg.* 122: 693, 1945.
13. Abbott, W. E., Pilling, M. A., Griffin, G. E., Hirshfeld, J. W., and Meyer, L.: Metabolic Alterations Following Thermal Burns. V. The Use of Whole Blood and an Electrolyte Solution in the Treatment of Burned Patients, *Ann. Surg.* 122: 678, 1945.
14. Langohr, J. L., Owen, C. R., and Cope, O.: Bacteriologic Study of Burn Wounds, *Ann. Surg.* 125: 452, 1947.
15. Connor, G. J., and Harvey, S. C.: The Pyruvic Acid Method in Deep Clinical Burns, *Ann. Surg.* 124: 799, 1946.
16. Cope, O., Langohr, J. L., Moore, F. D., and Webster, R. C.: Expeditious Care of Full-Thickness Burn Wounds by Surgical Excision and Grafting, *Ann. Surg.* 123: 1, 1947.
17. Cope, O., and Moore, F. D.: The Redistribution of Body Water and the Fluid Therapy of the Burned Patient, *Ann. Surg.* 126: 1010, 1947.

## CHAPTER 17

### THORACIC SURGERY

Rapid advances have been made in recent years in the surgical treatment of diseases of the thorax and its contents; current developments in this field of surgery have perhaps been greater than in any other. Painstaking and detailed anatomic studies, improvements in operative techniques, and experimental investigations have each played an important part, it is probable, however, that a more thorough understanding of the physiology of the chest and its contents in health and in disease has been the chief factor in making thoracic surgery feasible and safe. In no other field of surgery is a dependable working knowledge of applied physiology as indispensable as it is in thoracic surgery; well-planned and closely supervised preoperative and postoperative treatment is fully as important as proper choice and skillful performance of the operative procedure

#### Physiologic Considerations

Respiratory exchange depends upon maintenance of a sub-atmospheric pressure within the thorax. Normally the visceral and parietal pleural surfaces are in contact, with only sufficient fluid present to insure frictionless movement during respiration. During inspiration, the ribs are elevated, the thoracic cage expands, and the diaphragm contracts and moves downward. These movements increase the volume of the thoracic cavity and therefore decrease the intrathoracic pressure. As a result, air flows into the tracheobronchial tree until inspiration ceases. During expiration, the contracted respiratory muscles relax and the volume of the thoracic cavity decreases, forcing air out of the lungs.

If an opening is made in the chest wall, the inequality in pressure between the pleural cavity and the atmosphere causes air to enter the chest through the wound (sucking wound). The resulting pneumothorax produces collapse of the lung with consequent reduction in vital capacity and interference with respiratory exchange. The rate of entrance of air into the pleural

space is roughly proportional to the area of the opening; if the aperture is larger than the opening of the main bronchus, each inspiration draws more air into the pleural cavity than into the lung on the affected side. \*

In most cases, air passes into an opening in the chest wall on inspiration more easily than it is forced out on expiration. An increment of retained air therefore is added with each breath, the pressure within the involved side of the chest rapidly building up toward the atmospheric level. If the mediastinal structures are not fixed by fibrous or inflammatory adhesions but move freely, tension pneumothorax developing in this manner not only will cause collapse of the lung on the involved side, but also will cause displacement of the mediastinum, with partial compression of the lung on the opposite side and further reduction in vital capacity. Rising tension and increasing accumulation of air in the pleural space may result in this way from an abnormal opening either in the chest wall or in a bronchus, air leaking into the pleural cavity during inspiration but not escaping during expiration.

When the opening in the chest wall is large and air can pass in and out freely, collapse of the homolateral lung occurs at once and the mediastinal structures are shifted from side to side during the rapid forced respirations which follow the sudden reduction in pulmonary oxygenation. The swinging changes in intrathoracic pressure as well as the churning motions which result (mediastinal flutter) cause depression of respiratory exchange, interference with emptying of the great veins, and impairment of circulatory function. In consequence of the to-and-fro motion characteristic of forced respiration under these circumstances some of the residual air in the bronchial tree of the collapsed lung is forced back and forth across the bifurcation of the trachea, circulating uselessly between the two lungs and adding to the deficiency in respiratory exchange.

When inflammatory adhesions are present or have had time to develop, however, entrance of air into the pleural cavity through an aperture in the chest wall is limited by the extent to which the lung is bound to the parietal pleura. Little or no collapse of the lung may result, function continuing in those portions which are fixed to the chest wall by fibrous adhesions or plastic exudate. In like manner, maintenance of pulmonary

expansion by adhesions prevents displacement of the heart and great vessels; the presence of an opening in the chest wall under such circumstances causes little interference with cardiac function or respiratory exchange.

### Empyema

Postpneumonic infection of the chest cavity has become less common since chemotherapeutic and antibiotic agents have been used in treatment of pneumonia, although it still occurs occasionally. Pleural effusion with infection usually is secondary to pneumonia; putrid empyema, however, sometimes occurs following rupture of a lung abscess into the pleural cavity or into an interlobar space; and apparently sterile pleural effusions often appear in association with tuberculous infection of the lung. Postpneumonic empyema may be acute or chronic and varies in type and in clinical course according to the infecting organism responsible.

Empyema complicating streptococcic or influenzal pneumonia develops during the acute stages of the pneumonic process (synpneumonic empyema) and adds greatly to the severity of the primary disease. In such a case, the presence of a massive pleural effusion will cause compression of the lung and dangerously reduce the vital capacity, already seriously impaired by the consolidating pneumonitis. The effect of toxic absorption of bacterial products is added to the mechanical interference with respiration, so that development of empyema in the course of streptococcic or influenzal pneumonia is a serious and highly dangerous complication. The threat to life is most severe during the acute phase, when the purulent exudate is thin, profuse, and watery. During this stage effective drainage is difficult since some form of closed drainage must be used; an opening cannot be made in the chest wall for evacuation of pus because the lung is not fixed by adhesions and a sucking wound would result. Later in the course, when the pus thickens and adhesions begin to form, empyema originating from these types of pneumonia follows the same pattern as pneumococcic (metapneumonic) empyema and can be treated in the same way.

Empyema complicating pneumococcic pneumonia appears after the acute stage of the pulmonary disease has passed and

convalescence should be progressing (metapneumonic). The immediate danger to life therefore is less marked with metapneumonic empyema than with the synpneumonic type. In most cases of pneumococcic pneumonia, a small amount of exudate collects at the base of the pleural cavity; as a rule, this fluid gives little evidence of its presence during the course of the disease and is promptly absorbed without incident after recovery. Occasionally, however, the patient will recover from the pneumonia but will show evidence of persisting infection of moderate to severe degree. Delayed recovery of this type is due not to unresolved pneumonia but to increase in the pleural exudate, with development of an actively infected pleural effusion or empyema.

The purulent exudate in generalized empyema spreads throughout the pleural space of the involved side, from apex to base. Most of the infected fluid collects in the most dependent portion of the chest cavity, at which point drainage therefore will prove most effective. In the early stages of postpneumonic empyema the pleural exudate is relatively thin and cloudy; later in the disease the exudate becomes thickened and a heavy plastic fibrinopurulent deposit is laid down upon the visceral and parietal pleural surfaces. Unless complete evacuation of the exudate and prompt control of the infectious process are achieved rapidly, therefore, partial collapse of the lung and multiple pocketing of pus will result, with the eventual formation of small collections of densely encapsulated infected fluid that may be all but impossible to locate and drain. Sepsis, general debility, deformity of the chest, and chronic invalidism invariably follow the development of persistent chronic empyema. Atelectasis from external compression of the affected lung is soon transformed into obstructive atelectasis as the result of accumulation of bronchial exudate that cannot be cleared out by cough. *Pulmonary fibrosis then may result and the involved lung eventually loses its capacity for re-expansion and ventilation, often developing a significant degree of bronchiectasis.* These results of ineffectively treated empyema, although formerly very common, are now not often seen. The management of pyogenic infections of the chest cavity has been placed upon a sound basis by application of physiologic principles, first by the work of Graham and co-workers<sup>1</sup> at the close

of World War I and more recently by means of a more direct surgical attack, which has been made practicable by the development of improved anesthetic and operative techniques and of advances in preoperative and postoperative management.

**Treatment of empyema** includes removal of pus, prevention of pocket formation, control of active infection, complete re-expansion of the involved lung, prevention of complications, and restoration of normal pulmonary function and nutritional state. The goal to which every effort must be directed is the early re-expansion of the partially collapsed lung. Nothing should be permitted to interfere with this aim; any delay in re-expansion will lead to fixation of the lung in a partially collapsed position or to development of a bronchopleural fistula or both. No empyema is ever cured until the lung is in contact with the chest wall and adherent to it, with no intervening fluid. Each aspect of treatment is important and active therapeutic measures must be taken to insure full restoration to health as quickly as possible. Close attention to detail is necessary; it is a great deal easier to prevent the complications of empyema than to treat them after they have developed.

In the acute phase of the disease the exudate is thin and the lung is freely mobile within the chest cavity. Some form of drainage that will permit evacuation of pus and yet prevent simultaneous entrance of air into the chest must be used during this period. Pneumothorax superimposed upon acute empyema will prevent pulmonary re-expansion, add to the respiratory difficulty, encourage pocketing of pus in locations inaccessible for subsequent drainage, and promote chronicity of the infection. Because a layer of exudate is deposited on the pleural surface in acute empyema, absorption of air trapped in the pleural cavity proceeds at an extremely slow rate. Even relatively small amounts of air allowed to leak into the chest repeatedly during aspiration or closed drainage for acute empyema will collect in the apical region and interfere with drainage and with pulmonary re-expansion. Likewise, if rib resection with open drainage is performed too early in the disease, a sucking wound of the chest is created, collapse of the lung occurs, and interference with circulation and respiratory exchange may even be so severe as to be insupportable. Some form of closed drainage therefore must be used during the acute stages of empyema.

Opinions vary as to the best technique for closed drainage. The simplest but least effective method consists of *repeated thoracentesis* with aspiration of pus on each occasion until no more can be obtained or until the patient complains of pain as a result of rapid lowering of intrathoracic pressure by excessive suction. Thoracentesis is repeated as indicated at one- to three-day intervals until the pus becomes too thick to flow satisfactorily through a large aspirating needle, at which time closed drainage by catheter or open drainage by tube should be considered. Occasionally, repeated aspiration of the pleural exudate will effect a cure of the empyema; such a result is exceptional, however, and open drainage will be necessary in most cases.

Frequently, pleural exudate accumulates so rapidly during the acute stage that repeated thoracentesis will not afford sufficient drainage. Closed drainage by means of an *intercostal catheter* may then be effectively employed. The catheter is introduced under local anesthesia (with appropriate doses of morphine or a barbiturate for premedication), the interspace which will afford the most effective dependent drainage being chosen, usually the seventh or eighth just anterior to the posterior axillary line. A lower interspace is almost certain to be unsatisfactory, since the diaphragm rises as the exudate is withdrawn and will tend to block the catheter after a short time. The posterior axillary line is preferred because it provides optimal dependent drainage with the patient erect or supine.

After the selected site is anesthetized with procaine (1 per cent) down to the pleura, a small nick is made with a scalpel, thoracentesis is performed to verify the presence of pus, and the trocar is introduced as gently as possible, near the upper margin of the underlying rib. The obturator is withdrawn and a fenestrated catheter (18 to 24 French) is introduced promptly, the tip passing about 2 to 3 cm. into the pleural cavity. The trocar is then withdrawn, leaving the catheter in place. Insertion of too much tubing into the chest will push the tip up above the lowest level of the collection of pus; if too little tubing is inserted, however, the drainage openings may become blocked in a short time. The catheter is clamped tightly before passage through the trocar to minimize leakage of air into the chest; the clamp is not loosened or removed from the catheter until the closed drainage system has been connected.



## Water-syphon suction apparatus

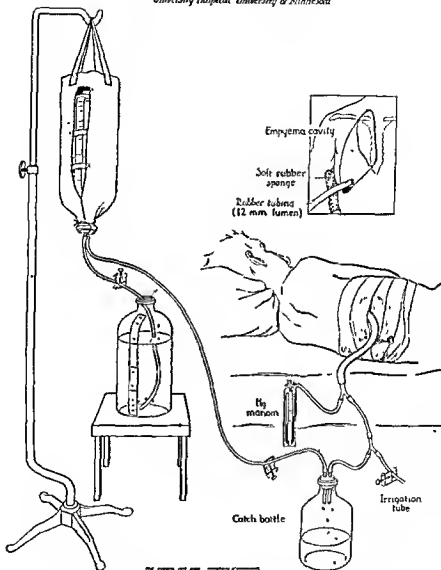
*University Hospital, University of Minnesota*

Fig 61 -- Wangensteen constant suction apparatus for closed drainage in empyema. A mercury manometer is attached to the tube leading from the chest to insure maintenance of a proper subatmospheric pressure within the cavity. Absence of leaks throughout the entire system is necessary to maintain water siphon system. (If leaks are present, a Sprengel water pump affords satisfactory suction.) (From Wangensteen, O. H.: *J Thor. Surg* 4: 399, 1935)

Leakage of fluid or air through the wound along the catheter can be minimized by application of a dressing of petrolatum gauze, by passing the catheter through a sheet of rubber dam<sup>2</sup> which is then fixed to the skin with rubber cement, or by use of a sterilized sponge rubber pad, such as a fine-grained bath sponge. In the latter method, which is much the best, a clamp is plunged through the center of the sponge, the end of the catheter is grasped with the clamp, and the sponge is passed down along the catheter until it can be taped snugly against the chest wall. A Y-tube connection is attached to the catheter and one end is connected either to a simple waterseal or to a continuous suction drainage apparatus (Figs. 61 and 62). The other end of the Y tube is kept tightly clamped and is used for direct aspiration as indicated.

The simplest system of closed drainage is the waterseal. One end of a rubber tube is connected to the intercostal catheter and the other end is placed below the fluid level in a bottle half filled with sterile water, placed on the floor or at least eighteen inches below the level of the intrathoracic end of the catheter. The drainage tube is attached securely to the neck of the bottle so that the open end cannot be displaced above the surface of the water. Rise of intrathoracic pressure during expiration encourages discharge of pus into the drainage bottle; during inspiration water rises in the tube for several inches. This alternating movement of water in the tube with each respiration indicates that the drainage system is operating satisfactorily. Absence of such movement may indicate that an air leak is present, that the tube is plugged, that the intrapleural drainage openings are blocked, or that the empyema cavity has become so walled off by fibrinous exudate that pressure variations during respiration are no longer transmitted.

The constant gastric suction apparatus of Wangensteen (Fig. 17) can be adapted<sup>3</sup> to provide similar constant suction drainage for evacuation of empyema fluid (Fig. 61). In many hospitals the gastric suction drainage apparatus is used without modification for constant suction drainage of the pleural cavity. Better control of aspiration is obtained, however, if a manometer is interposed in the system so that the negative pressure within the thorax can be maintained constantly within a range of -10 to -25 cm. of water. Suction is regulated by raising or lowering

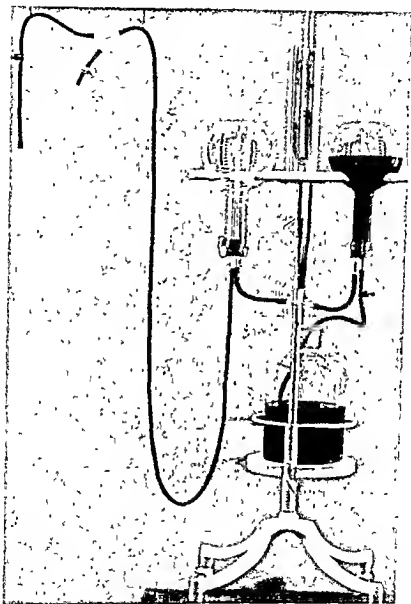


Fig. 62 — Modified double Wangensteen portable suction apparatus for draining and obliterating the pleural space following intrathoracic operations. A manometer connected with the tubing between the two upper flasks aids in determining the amount of suction applied to the pleural cavity. (From Adams, W. E.; *Surgery* 10: 1005, 1941.)

the lower bottle of the siphon system. Various modifications of the suction apparatus have been developed in different medical centers; some of the systems used are adaptations<sup>2</sup> of the automatic tidal drainage apparatus originally suggested by Hart and provide controlled irrigation as well as suction drainage. Others are simple variations of the Wangenstein suction apparatus and provide constant suction only. As a rule, the simplest forms of apparatus give the best results. Unless the attendants are specially trained, they are likely to be confused by complicated systems which require close attention. The commonest errors in care of the constant suction apparatus are failure to notice promptly the absence of oscillation of the water column with respiration, failure to keep the reservoir of the siphon system properly filled with water, and failure to keep the end of the lower tube of the siphon system fixed below the surface of the water. Also, in occasional instances, the wrong tube of the suction reservoir has been connected to the chest catheter, with a resultant hydrothorax from backflow of water into the chest by gravity.

Strong suction is not necessary during closed drainage unless a bronchopleural fistula develops, with constant leakage of air into the pleural cavity. In such a case the suction provided by siphon drainage may be insufficient to remove the constantly accumulating air; a suction water pump (Sprengel) or an electric suction motor will prove more successful.

Closed drainage in empyema is continued as long as exudate drains freely through the tube and pressure variations with respiration are visibly transmitted to the fluid level in the manometer or the waterseal bottle. As the exudate thickens, the intercostal catheter becomes blocked more frequently and drains less efficiently; flakes and clots of fibrin are seen in the draining pus, which becomes thicker and more viscid. At this stage it is safe to discontinue intercostal drainage and to institute open drainage by *rib resection*. Occasionally, when closed drainage is prolonged beyond the point at which the exudate thickens, fibrin is precipitated from the pus and is deposited in the pleural cavity in large masses, leaving a thin milky fluid containing solid flakes of fibrin to be discharged through the catheter. So much difficulty is encountered in keeping the catheter clear under these circumstances, however, that the proper decision to perform open drainage is soon made. Closed or airtight drainage is

not necessary for more than three weeks after onset of acute empyema.

Before rib resection is done, roentgenograms in at least two planes are made to localize the pus as accurately as possible, physical examination of the chest is performed, and thoracentesis is done to determine the lowest point in the posterior axillary line at which pus is obtained. Usually the rib just above the location of the intercostal catheter is chosen for resection, and a segment two to three inches in length is removed subperiosteally in this line. Loculated pockets are broken up and gelatinous masses of fibrin are swept out by insertion of a finger into the opening. A flanged soft rubber tube at least one inch in diameter is inserted. A safety pin is fixed to the external portion of the tube, both to prevent its retraction into the pleural cavity and to permit its localization by roentgenogram in case it should be lost in the wound. Following operation the patient is instructed to lie on his back or on the affected side, and the head of the bed is elevated to promote drainage by gravity. Dressings are changed daily and the tube is allowed to remain in place until the empyema cavity has healed and closed completely up to the tube, at which time a smaller tube may be substituted. Shrinkage of the cavity is observed weekly by introduction of a measured amount of sterile normal salt solution through the tube or by x-ray visualization following introduction of iodized oil; little information can be gained simply by physical examination. Although many surgeons recommend repeated irrigation of the cavity to encourage removal of fibrin masses, this procedure is subject to the serious disadvantage that secondary infection may result. Final healing of the cavity is insured by substitution of progressively smaller drainage tubes, to be withdrawn gradually at intervals of several days. Healing of the cavity from the bottom outward results, and the tube is not permanently withdrawn until the remaining cavity is shallow and has a capacity of less than 15 cubic centimeters.

An alternative plan<sup>4</sup> which has been used with excellent results is to employ repeated aspiration during the most acute stage of the illness and then to perform rib resection with introduction of a large tube (one-fourth inch in diameter) fitted into the wound snugly enough to be airtight and connected immediately to a constant suction drainage apparatus. An air-

tight fit is necessary in the pleural opening only; the wound in the chest wall is packed with petrolatum gauze and the tube is passed through a rubber sponge dressing (p. 555). This method will afford highly satisfactory results in the hands of those who are skilled in its use; if improperly performed, it may permit establishment of a troublesome pneumothorax, leakage of pus around the tube with development of wound infection, or respiratory embarrassment consequent upon rapid evacuation of a large quantity of fluid from the chest. The latter disadvantage can be avoided if the tube is clamped before insertion into the chest and is subsequently released at intervals of four hours to permit withdrawal of pus in amounts of 250 c.c. until the chest is cleared. The tube is then attached to a waterseal or a suction drainage apparatus and is allowed to remain unclamped.

*Sulfonamides* are of no constant value when applied locally in acute or chronic empyema; systemic chemotherapy, however, is useful for prophylaxis and treatment of the accompanying pneumonitis and locally invasive infection. *Penicillin* is the most valuable single antibacterial drug in the treatment of empyema; it is administered both locally and systemically in large dosage. Attempts have been made to treat acute empyema by repeated aspiration of pus and simultaneous injection of penicillin into the infected pleural cavity, supplemented by penicillin given systemically. Although occasional cures may be obtained by this method, the usual result is that active infection is controlled and even the pus may be sterilized, but the problems<sup>6</sup> of drainage of exudate, obliteration of the empyema cavity, and re-expansion of the lung still remain. Although penicillin cannot be depended upon to cure empyema, it will minimize bacterial growth, spread of infection, and sepsis and consequently will produce improvement in general condition. Penicillin can be injected directly into the empyema cavity in amounts of 50,000 to 100,000 units in sterile normal salt solution following each thoracentesis (every one or two days) and should be administered by parenteral injection in doses of 40,000 to 100,000 units every three hours. Large doses are necessary when the infection is becoming chronic or when it is mixed in type; empyema caused by the gram-positive cocci alone will respond to ordinary doses of penicillin, but very large amounts of the

drug are required in mixed infections containing organisms which do not respond to penicillin or which inactivate it.

The patient is required to exercise actively in bed after the acute stage of the disease has subsided. Deep-breathing exercises every hour will help to prevent atelectasis and encourage re-expansion of the lung. Blow bottles have been used for years in the treatment of empyema in the hope that forced inspiration and expiration will promote pulmonary expansion. It is probable, however, that obliteration of the empyema cavity is accomplished by the progressive formation of granulating adhesions between the parietal and visceral pleural surfaces, this process being favored chiefly by prompt and efficient removal of the purulent exudate which serves to keep the two pleural surfaces apart.

Fluids are administered either orally or parenterally in quantities sufficient to maintain the urinary output at 1,000 to 1,500 c.c. daily. Since infection as extensive as empyema causes a continued loss of large amounts of protein in the form of purulent exudate, a high intake of dietary protein is necessary. A satisfactory diet should include from two to four times the basic daily requirement of 1 Gm. of protein per kilogram of body weight per day. A high protein, high carbohydrate, low fat diet is ordered to supply at least 50 calories per kilogram of body weight daily, as soon as the patient is able to take this much food. Most of the protein can be supplied as intermediate nourishments of skim milk powder, milk protein, or protein hydrolysate (15 to 45 Gm.) in water every four hours. During the acute stage of empyema, protein hydrolysate can be administered intravenously in sufficient quantity to supply the equivalent of 50 to 100 Gm. of protein each day. Therapeutic doses of vitamins B complex and C are given either orally or parenterally, and the red blood cell count and hematocrit values are followed closely. Transfusions of blood are of the greatest value in patients with acute or chronic empyema; enough blood is administered to keep the hemoglobin and the total blood volume near the normal levels.

If acute empyema is recognized promptly and treated properly, a complete cure should be obtained in most cases within four to six weeks. Delayed or inadequate treatment will result in chronicity of the infection with the formation of pockets of

pus throughout the chest that will require repeated attempts at drainage by rib resection. Thoracoplasty eventually may be necessary to secure obliteration of thick-walled cavities in long-standing cases. Common causes of chronicity in pyogenic empyema include (1) delay in institution of treatment; (2) inadequate drainage through too small a thoracentesis needle or intercostal catheter or by resection of an insufficient length of rib; (3) location of the drainage site at too high a level, permitting pooling of pus below the outlet; (4) location of the drainage site at too low a level, permitting obstruction of the opening by the diaphragm, which rises as the empyema fluid is withdrawn and pulmonary expansion returns; (5) deposition of fibrinous masses throughout the pleural cavity, encouraging pocketing of pus in inaccessible areas, prolonged collapse of the lung, and pulmonary fibrosis; (6) development of a bronchial fistula as a result of inadequately drained pleural infection with secondary subpleural pulmonary abscess; (7) presence of a foreign body in the chest (often a portion of drainage tube which has been lost); (8) a mixed pyogenic and tuberculous empyema; (9) presence of an undiscovered undrained pocket of pus, and (10) general debility and malnutrition.

With improvement in methods of preoperative and postoperative care, interest has been renewed in *pulmonary decortication* in treatment of early chronic postpneumonic empyema. The operation recently has proved to be as successful in treatment of selected cases of this type as in infected traumatic hemothorax. Decortication should be considered early in the course of multilocular or total empyema, especially with collapse of the upper lobe, with an unsatisfactory response to more conservative therapy. If decortication is performed four to six weeks after onset of empyema, the investing exudate on the visceral pleura is sufficiently well organized to permit development of a line of cleavage and removal as a definite layer. When more than eight weeks has passed, however, fibrous organization will have occurred between the exudate and the pulmonary pleura and removal of the offending layer will be a more difficult task, involving tearing of the pleura from the underlying lung at many points of dense adherence, with resultant bleeding and leakage of air. The operation therefore is most successful in early cases. It is performed under intratracheal anesthesia through an in-



cision along the fifth interspace or through the bed of the resected fifth rib. The layer of exudate is stripped by blunt dissection from the pulmonary pleura, particular attention being paid to the apical region and the diaphragm; the exudate covering the parietal pleura is left undisturbed unless large masses are present. Re-expansion of the freed lung should occur promptly. Procaine is injected paravertebrally to block the intercostal nerves immediately above and below the incision, and penicillin (100,000 units in 20 c.c. of sterile normal salt solution) is left in the pleural cavity when the incision is closed. Bronchoscopic aspiration of the tracheobronchial tree is performed before the patient leaves the operating room. Sanger<sup>4</sup> advises the use of three mushroom catheters (28 to 34 French) intercostally to provide drainage of the pleural space during the early postoperative period. The tips of the catheters are cut off to provide a small remaining flange; one catheter is inserted through the second interspace in the midclavicular line, one in the eighth interspace in the posterior axillary line, and one in the costophrenic sulcus in the anterior axillary line.

Each catheter is connected to a separate waterseal or constant suction apparatus and the posterior catheter is kept clamped for six hours to prevent loss of the penicillin. The anterior catheter provides an outlet for air which may leak through a torn pulmonary pleural surface; the lower catheters, particularly the posterior one, will drain blood and exudate. Full expansion of the lung should occur within twenty-four to forty-eight hours after operation. Physical examination of the chest is done routinely twice each day and a roentgenogram is secured by the third day to detect any undrained accumulation of air or fluid, which is then removed by thoracentesis. It is of the greatest importance to secure immediate and complete re-expansion of the decorticated lung to prevent recurrence of empyema. The anterior catheters are removed when pulmonary re-expansion is complete; the posterior catheter is retained for ten to fourteen days.

Each waterseal is inspected several times daily to insure against block; the water column should be noted to rise and fall with each respiration. If a catheter is plugged by exudate or blood clot, efforts are made to clear it by aspiration with a syringe; several cubic centimeters of sterile normal salt solution

may be injected if necessary. Evidence of dyspnea may indicate pulmonary collapse from air in the pleural cavity or hemothorax due to leakage of blood from adhesions torn at operation; attempts are made to open the blocked catheter, the chest is examined carefully by percussion and auscultation, and a portable x-ray film is secured at once. Collections of blood or air are evacuated by thoracentesis; if clotting has occurred, it may be necessary to return the patient promptly to the operating room and to remove the blood and control the bleeding by thoracotomy under general anesthesia. It is scarcely possible to overemphasize the importance of maintaining a close and constant watch upon the drainage tubes and upon the patient's general condition following decortication; postoperative hemorrhage is not an uncommon occurrence and it may prove rapidly fatal unless treated promptly.

If mucus accumulates in the bronchi during the early postoperative period, tracheobronchial catheter suction (p. 369) is performed without delay; bronchoscopy is done if catheter aspiration is not fully effective at once.

Other measures following decortication are similar to those employed following any other major intrathoracic procedure. The patient is placed supine or on the operated side, oxygen is administered by intranasal catheter or by tent if the weather is hot, transfusions of blood are supplied in sufficient quantity to maintain normal hemoglobin and hematocrit levels, penicillin is given intramuscularly in doses of 40,000 units every three hours for five days, and proper dietary, fluid, and vitamin intake is insured. The patient is made to move about frequently, with complete change of position every hour when awake, deep-breathing exercises are undertaken every hour, and the arms and legs are exercised at frequent intervals.

### Traumatic Wounds

The principles of treatment of thoracic wounds and injuries have been more clearly drawn and established following military experience in World War II. The extremely low mortality and morbidity rates among soldiers who sustained wounds of the chest were due in great measure to the availability of qualified surgeons and anesthetists in fully equipped field hospitals and

portable surgical units close to the zone of combat. Seriously wounded patients were often received in an hour or less after injury and were treated for shock, prepared for surgery, and operated upon by surgical teams, each of which was organized and equipped as a functioning unit. After closely supervised convalescence for a sufficient period, patients with chest injuries were transferred to larger installations designated as thoracic surgery centers, where specialized care was continued until recovery. Many lives were saved by this plan of care and much information has been gained about treatment of thoracic wounds.

### LACERATED WOUNDS

Lacerated wounds of the chest wall and compound rib fractures are treated by débridement, especially if sharp spicules of rib are piercing the pleura. Sucking wounds of the chest, even if extensive, may require nothing more than surgical cleaning and closure; thoracotomy is not necessary if no other indication is apparent. It is to be remembered that leakage of blood into the pleural cavity occasionally may arise from a partially severed intercostal or internal mammary artery rather than from a wound of the thoracic viscera, particularly if a comminuted rib fracture is present. Thoracentesis is performed at frequent intervals as necessary to remove accumulations of blood and serum during early convalescence from wounds of the chest.

Continuing hemorrhage and unrelieved respiratory obstruction constitute the chief indications for immediate surgery in thoracic injuries as well as in injuries elsewhere in the body. More specifically, prompt open thoracotomy is indicated in the presence of (1) severe traumatic injury involving several adjacent ribs and intercostal bundles; (2) penetrating thoraco-abdominal wounds; (3) significant injury to the mediastinal structures; (4) hemothorax with continuing bleeding; (5) hemothorax with a massive intrapleural clot causing pulmonary collapse, mediastinal shift, and respiratory distress; (6) tension pneumothorax due to persisting leakage of air from a large wound of the lung; and (7) large fragments of metal (1.5 cm. or more in diameter) or fragments of shattered rib, shreds of clothing, or other foreign material buried in the lung or in the pleural cavity.

Emergency treatment of patients with thoracic wounds includes replacement of lost blood and treatment of shock, relief of dyspnea or respiratory obstruction, and care of the wound. Dyspnea may be due either to pulmonary collapse as a result of blood and air in the pleural cavity or to tracheobronchial obstruction from accumulated mucus or blood.

Each laceration of the chest wall is examined carefully for evidence of passage of air; a narrow wound may permit sucking only with deep respiration or when the thorax is turned or twisted in certain positions. Sucking wounds are immediately packed or covered with any sterile dressing material available until repair can be done. X-rays are taken in at least two planes.

Intrapleural collections of blood or air that are large enough to be detected on physical examination will usually cause definite respiratory embarrassment, dyspnea, cyanosis, or mediastinal shift; withdrawal by thoracentesis is done promptly if these symptoms are present and repeated as often as necessary. Large needles up to 15 gauge may be needed if clotting has begun. Aspiration is discontinued if the patient complains of pain or tightness from too rapid reduction of intrathoracic pressure in the presence of a compressed or atelectatic lung; a few cubic centimeters of air are reinjected to restore comfort, and aspiration is repeated later as needed.

Operation is less urgent in thoracic wounds than in abdominal injuries. Penetrating wounds of the gastrointestinal tract are likely to cause peritonitis; the immediate problem in thoracic injuries, however, is primarily mechanical. If respiratory distress is relieved by removal of collections of air or blood from the pleural cavity or by aspiration of mucus or blood from the tracheobronchial tree, as much time as necessary may be taken to prepare the patient for operation.

At the completion of operation, procaine block of the intercostal nerves above and below the site of operation is performed, the lung is re-expanded by positive pressure, and penicillin (100,000 units) is left in the pleural cavity. Before the patient is removed from the operating room, anterior thoracentesis is done to remove all remaining air and bronchoscopic aspiration is done to clear the tracheobronchial tree. The intravenous injection of atropine, 0.6 mg. (gr. 1/100), has been advised<sup>7</sup> before bronchoscopy upon a patient recovering from

anesthesia to prevent a possible vagovagal reflex. Oxygen is given constantly as a routine measure in all cases following operation.

The most important considerations during the postoperative period are to keep the pleural cavity free of air and fluid and to keep the tracheobronchial tree clear of mucus. Routine postoperative drainage of the pleural cavity following thoracotomy is generally best accomplished by intercostal catheters (p. 562), although some surgeons prefer aspiration by thoracentesis repeated as indicated.

**"Wet Lung."**—Respiratory distress occurring shortly after a thoracic injury or operation may be due solely to accumulation of mucus and secretions throughout the bronchial tree. Since coughing causes pain in the wound, the patient tends to cough gently at frequent intervals, bringing up small amounts of secretion from the trachea but never effectively clearing the lower bronchi. In this state, termed "wet lung" by Brewer and associates,<sup>8</sup> the bronchial tree has been likened to a full cup with a little exudate splashing over the top on frequent occasions. This condition should be suspected when the patient exhibits a continual annoying cough, always moderately productive, with an asthmatic type of dyspnea and either dry or bubbling râles widespread on auscultation. Moderate fever and toxicity are present; x-ray examination is likely to be inconclusive since the atelectasis may be patchy and diffuse. Treatment includes (1) thoracentesis if collections of air or fluid are present; (2) gastric aspiration if the stomach is distended; (3) procaine (1 per cent) block of the intercostal nerves above, below, and in the distribution area of the wound if coughing causes pain; (4) frequent change in position, with enforced deep-breathing exercises and coughing; and (5) administration of carbon dioxide inhalations, preferably by means of a small funnel discharging 100 per cent carbon dioxide, held several inches from the patient's face for several breaths. Morphine should not be given to relieve pain in the wound; intercostal block will reduce pain enough to permit effective coughing and clearing of the bronchi. If coughing is not fully effective even after successful nerve block, tracheobronchial aspiration is performed by catheter suction (p. 369) or by bronchoscopy. Continued pro-

fuse bronchial secretion continuing even after proper suction aspiration may be the result of alveolar and bronchiolar damage from prolonged anoxia. In such a case the prompt administration of 100 per cent oxygen by means of a Boothby mask is often helpful; gentle positive pressure is of value if pulmonary edema is present.

### TENSION PNEUMOTHORAX

Tension pneumothorax may result from a wound in the pulmonary parenchyma or in a portion of the bronchial tree. Air escapes into the pleural cavity during inspiration but cannot return through the same opening during expiration. The intrapleural tension and pulmonary collapse increase with each respiratory cycle, causing mounting respiratory distress.

As a rule the defect will heal spontaneously if an outlet is provided for the constantly leaking air. If the leak is small, repeated aspiration may suffice; if large, intercostal waterseal drainage is used. A catheter is passed through the second or third interspace just outside the midclavicular line to permit escape of air, and a similar catheter may be passed through the seventh or eighth interspace in the posterior axillary line to permit escape of the serous or serohemorrhagic exudate which characteristically forms in traumatic injuries. Each catheter is connected to a separate waterseal apparatus; suction is not applied for several days, to allow healing to occur in the stationary, partially collapsed lung. After the fifth day, constant gentle suction (-10 cm. of water) may be instituted to encourage re-expansion.

Physical examination of the chest is performed at least twice daily and a roentgenogram is taken on the third day. If the catheters become blocked or dyspnea develops, physical and x-ray examinations are made at once; thoracentesis will probably be required for removal of accumulated air or fluid. Rapid withdrawal of air by thoracentesis under these circumstances may cause pain and tightness in the chest; aspiration is stopped and enough air is reinjected to restore comfort. The catheters are cleared or, if too small, are replaced with larger ones. Great care must be taken to insure that the drainage tube is never allowed to come above the surface of the water in the water seal bottle or the lower bottle of the siphon system. Removal of the drainage catheters before healing is complete will

result in reappearance of the tension pneumothorax, as long as two weeks may be required for healing of a large bronchopleural fistula.

When an acute emergency arises and a trocar and catheter are not available for relief of tension pneumothorax, a thoracentesis needle can be introduced in the proper location and a rubber finger cot tied securely over the hub of the needle. A slit is made in the end of the finger cot to form a flap valve, permitting exit of air but not entrance.

### HEMOTHORAX

Hemothorax that causes respiratory distress is treated by immediate aspiration without delay. Large collections of blood in the pleural cavity that do not cause dyspnea are allowed to remain undisturbed for thirty-six to forty-eight hours, after which they are removed by thoracentesis. Small collections of blood detectible on x-ray but not on physical examination are allowed to absorb spontaneously.

Methods formerly practiced but no longer approved include either allowing a large hemothorax to be absorbed spontaneously or removing it by aspiration and injecting an equal amount of air. Current practice favors prompt removal of significant collections of blood to minimize subsequent adhesion formation, to reduce incidence of post-traumatic empyema, and to restore normal pulmonary function as promptly as possible. Injection of air following removal of blood was practiced to keep the lung collapsed and insure healing of the lacerated blood vessels; however, renewal of bleeding does not occur if an interval of one to two days is allowed to pass before the hemothorax is aspirated. Moreover, the prolonged pulmonary collapse which follows injection of air tends to prevent full re-expansion later and permits extension of infection throughout the entire pleural cavity if post-traumatic empyema should occur.

Thoracentesis is repeated as required to keep the accumulation of blood and serous fluid at a minimum; if not productive of discomfort, up to a liter of blood and air can be removed on each occasion until full pulmonary re-expansion occurs. Large collections of clotted blood which cannot be removed by aspiration with the largest needles are removed promptly by open thoraco-

tomy to forestall the development of infection and empyema. Catheter suction is likely to be ineffective also if thoracentesis is unsuccessful. Penicillin is administered systemically in the usual dosage and is injected into the pleural cavity (100,000 units in 20 c.c. of sterile normal salt solution) following each thoracentesis. Blood is administered by transfusion in sufficient quantity to maintain normal hemoglobin and hematocrit levels. The chest is examined routinely twice each day and frequent x-ray examinations are made. Sudden development of dyspnea or distress usually signifies pulmonary collapse due to collection of tracheobronchial mucus or to accumulation of a large amount of air, fluid, or clotted blood in the chest.

Removal of blood by aspiration is often incomplete, a continuous layer of clot and fibrin remaining adherent to the pleural surfaces of the entire hemi-thorax. Organization occurs within three to five weeks, the outer (pleural) aspect of the clot being transformed into a firm fibrous layer while the center remains amorphous and jellylike. Progressive thickening develops and by the seventh week the organized outer coat has formed a thick fibrous sheath over the pleural surface of the entire lung. As scar tissue growth proceeds beyond this point, the investing layer becomes densely adherent and irremovably attached to the lung, which is then fixed in partial collapse. Such residual collections of blood following hemothorax may remain clean but are likely to develop infection of varying degrees of severity, sometimes producing symptoms typical of empyema with formation of frank pus.

Although the advantage of early removal of the clot in such cases has been recognized for some years, the operation formerly was not generally feasible and infected hemothorax was treated in much the same way as postpneumonic empyema. During World War II, decortication for hemothorax was performed with the greatest possible success and has become the procedure of choice in cases with persisting intrapleural clot. Samson and associates,<sup>9</sup> who reported the earliest and most extensive use of this operation in military hospitals, advocate pulmonary decortication in the late treatment of hemothorax if the lung remains partially collapsed for a month after injury, especially if the apex is compressed and aspiration has been unsuccessful. Decortication is best performed when the hemothorax is from four to six



weeks old, at which time the investing layer of clot has become firmly organized but is not yet densely adherent to the pleura. The technique of operation and postoperative care in decortication for hemothorax are essentially the same as in decortication for empyema (p. 561).

Treatment of hemothorax is more complicated when infection and frank pus formation are present. If the empyema is small in extent, repeated aspiration is performed until the pus becomes thick, when open drainage by rib resection is done. A more extensive infected hemothorax producing as much as 25 per cent collapse of the lung will progress into typical chronic empyema if treated by the usual methods. Decortication has given excellent results in such cases also, drainage by thoracentesis being done until the pus is thick and then removal of the infected enveloping clot by open thoracotomy as in the clean cases. Interval drainage by intercostal catheter rather than by thoracentesis is unlikely to be successful because of the thickness of the infected blood clot. Measures of care following operation do not differ from those in uninfected cases.

### Elective Surgery

The success of thoracic surgical procedures is directly dependent upon the adequacy of preparation and aftercare. Alexander<sup>10</sup> has stated that "countless patients have failed to recover their health or have died following technically perfect thoracic operations solely because the surgeons failed to apply with intelligent understanding those preoperative and postoperative measures that are based on a thorough familiarity with thoracic physiology and pathology and with the behavior of diseases of the chest."

Before operation is undertaken, studies of the patient's nutritional state, respiratory reserve, and cardiovascular, hepatic, and renal functions are made; such investigations are equally as important as detailed diagnostic studies of the pulmonary pathologic condition. Patients requiring this type of surgery are likely to be debilitated to some degree by chronic pulmonary disease, infection, or atelectasis, and anemia, hypoproteinemia, and avitaminosis also are often present.

General preoperative measures required for improvement of the patient's condition are similar to those employed before other major operations. Complete blood studies are made at frequent intervals, and transfusions of whole blood are given until the red cell count, hemoglobin, hematocrit, and blood volume approach normal. Because thoracic operations reduce the amount of pulmonary tissue available for oxygen exchange, even a moderate reduction of hemoglobin is dangerous.

A high protein, high carbohydrate, low fat, high vitamin diet supplying 3,500 calories daily should be ordered, and close check is kept to be sure that the patient takes his food. Supplementary feedings of biologically complete protein are of great value in patients with chronic pulmonary infection, most of whom show appreciable degrees of wasting of body tissues. Intermediate nourishments of powdered skim milk or of commercially available milk protein concentrates can be given in quantities of 1 or more ounces in water three or more times daily. Skim milk powder (fat free) contains approximately 35 per cent protein; milk protein concentrates are much more expensive but provide more than twice as much protein per unit of weight. Either preparation is satisfactory; both are fully as effective as protein hydrolysate and are less expensive and more agreeable to take. High protein feeding is of considerable importance in patients of this type, and a firm and persistent effort should be made to keep them interested in taking the supplements. Hypoproteinemia will respond most quickly to transfusion of blood; infusions of protein hydrolysate and feeding of high protein diet will compensate for continued nitrogen loss and promote restoration of depleted body tissues over a period of days or weeks but will produce little immediate change in plasma protein values. Therapeutic doses of vitamins, especially B complex and C, are administered orally if the preoperative period is long or parenterally if early operation is planned. Hypoprotebinemia may be found in many cases, particularly if bleeding has occurred; prothrombin time determination is done routinely before operation and vitamin K is administered when necessary.

Bed rest is ordered, with bathroom privileges and short periods of mild exercise during the days before operation. Confinement to bed until operation is not desirable except in patients with hemoptysis, since prolonged recumbency may contribute to

accumulation of bronchial secretions, pulmonary atelectasis, venous thrombosis, and depression of muscle tonus and general condition. Infections in the mouth, throat, and sinuses are cleared, dental cavities are filled if possible, and skin inflammations are treated. Estimations of the cardiac reserve, hepatic and renal functions, and vital capacity are made. Much information concerning cardiac and pulmonary reserve can be gained by noting the patient's pulse and respiratory rates before and after moderate exercise; poor general health and poor muscle tonus will reduce the exercise tolerance and vital capacity and foreshadow a poor response to operation, even though visceral functions appear normal by laboratory test.

Responsibility for care of patients with significantly reduced pulmonary reserve should be shared between the surgeon and an internist. After detailed evaluation of every aspect of the patient's condition, decisions can be made as to whether the projected operation will impose too much strain on the depressed pulmonary and cardiac functions and whether further delay with special methods of preparation will improve the patient's condition enough to make him a better operative risk.

**Special Preoperative Studies.**—*X-ray examinations* of the chest are made in several planes and in stereoscopic views to determine as accurately as possible the location, extent, and degree of the pathologic process. Comparisons are made with earlier x-ray films; a series of roentgenograms made at intervals over the course of the patient's disease is of the greatest diagnostic value; if such plates were taken at other hospitals, an effort should be made to secure them for study.

*Diagnostic bronchoscopy* is performed in all patients with intrathoracic disease arising in or involving the bronchi. Pus or exudate can be obtained for laboratory study from the bronchus through which it drains. Tumors, ulcers, foreign bodies, and areas of stenosis located in the main bronchi and primary subdivisions of the lower lobes can be visualized in most cases and a biopsy can be secured, when indicated. The highly skilled bronchoscopist can frequently recognize evidence of infiltrating lesions of the lung which do not present themselves within the lumen of the bronchus by the presence of fixation and immobilization of the bronchial wall. It should be noted, however, that while biopsy of an endobronchial lesion should be performed to establish a

pathologic diagnosis, no delay should be permitted for this reason alone<sup>11</sup> if definite evidence of neoplasm is present and the patient is otherwise in good condition for exploratory thoracotomy and possible pneumonectomy.

*Bronchographic studies* are made in all patients with bronchiectasis in whom lobectomy is considered. Since early bronchiectatic changes may not be evident in the plain x-ray film or in the lung itself as seen at operation, the entire bronchial tree of each lung is visualized with radiopaque oil before operation is planned. Bronchography is of value also in the diagnostic study of lesions which cannot be visualized by bronchoscopy, such as those occurring in the upper lobe bronchi or in the peripheral portions of the lung tissue.

Bronchographic examinations are best done under fluoroscopic control, the iodized oil being introduced through a tracheal catheter. Only enough of the oil is used to indicate the outlines of the bronchial tree; larger amounts will overfill the saccular dilations and interfere with interpretation. Following satisfactory bronchography, operation is postponed until all the iodized oil has been cleared from the lungs. The substance acts as a foreign body and, if allowed to remain in the bronchi, may contribute to the development of postoperative pulmonary atelectasis in the remaining lung tissue.

*Artificial pneumothorax* preliminary to x-ray examination of the chest frequently makes it possible to determine whether the lesion is in the lung, the mediastinum, or the chest wall, the air being utilized as a contrast medium. Pneumothorax also is used preoperatively to demonstrate the presence of pleural adhesions before thoracotomy for pulmonary neoplastic disease to permit choice of the most advantageous incisional approach.

Induction of artificial pneumothorax as a routine preparation for pneumonectomy is advocated by some thoracic surgeons although not practiced by all. Rienhoff<sup>12</sup> states that this measure (1) serves as a therapeutic test to determine whether the remaining lung will suffice to support life, (2) facilitates pneumonectomy by reducing the size of the affected lung, (3) accustoms the patient to increased intrapleural pressure and reduces the danger of pleural shock at operation, and (4) reduces blood flow through the diseased lung, diminishing the extent of the sudden strain on

the right heart at operation when the pulmonary vascular bed is suddenly reduced.

Pneumothorax, however, is contraindicated in preoperative study or treatment of patients with pulmonary suppurative disease, particularly lung abscess; there is distinct danger that the adherent lung may be pierced or that the sudden rise in intrapleural pressure may cause tearing of pleural adhesions, with damage to the underlying pulmonary parenchyma and possible leakage of pus from the area of infection. There is little reason from any standpoint to employ artificial pneumothorax in patients with chronic suppurative disease of the lung, since pleural adhesions are invariably present and will prevent effective collapse.

*Aspiration* by thoracentesis is of the greatest value in diagnosis and treatment of pleural infection (empyema) and is indicated also for study of nonpyogenic pleural exudates. The aspirated fluid is examined by smear, culture, and chemical study; if tuberculosis is a possibility, guinea pig inoculation is performed. Thin serohemorrhagic fluid should arouse suspicion of malignant disease with metastases to the pleural surface; search is made also for tumor cells in the centrifugalized fluid.

Aspiration of an undiagnosed pulmonary parenchymal lesion which produces a shadow on x-ray is not advisable, even for the purpose of securing a biopsy. The danger is too great that purulent infection will be carried to the pleural cavity and to previously unaffected areas of the lung or that malignant cells will be implanted on the pleural surfaces.

By use of these methods of study, together with repeated and thorough examinations of sputum<sup>12</sup> collected both by expectoration and by direct bronchoscopic aspiration, a positive diagnosis can be reached in most cases. Unless there is strong presumptive evidence that a bronchogenic carcinoma is present, diagnostic examinations can be continued with profit over a period of as long as three weeks if necessary to reach a conclusion. It is worth while to decide whether a circumscribed pulmonary shadow is due to tuberculosis, pyogenic infection, or neoplasm, since inflammatory disease is treated by limited resection with conservation of uninvolved lung tissue, while carcinoma demands total pneumonectomy. Graham<sup>13</sup> has emphasized that in patients with bronchogenic carcinoma, evidences of inoperability should

be sought before thoracotomy is performed. Signs and symptoms of incurability in malignant pulmonary disease include presence of serosanguineous pleural fluid or of demonstrable metastases, paralysis of the homolateral vocal cord or leaf of the diaphragm, severe pain in the thoracic wall or down the arm from invasion by tumor growth, or bronchoscopic evidence of involvement of the trachea by tumor. Not all of these signs are currently regarded as contraindication to palliative resection for pulmonary malignancy, however.

*Postural drainage* is necessary in both the nonsurgical and the preoperative treatment of bronchiectasis and productive pulmonary abscess. While the cavities can be emptied of pus by bronchoscopic aspiration, it is never possible or desirable to perform this procedure often enough to keep the bronchial tree clean. Postural drainage, on the other hand, can be carried out by the patient without discomfort as often or for as long a time as necessary during the day and will be perfectly effective, as a rule, if properly done.

Postural drainage depends mechanically on maintaining the affected bronchi at a higher level than the trachea for a long enough time to allow all the exudate to flow out by gravity. It is performed most simply by bringing the patient over the side of a high bed or end of a high table so that the thighs remain on the bed and the trunk is inverted directly downward, with the hands or elbows on the floor. A basin is used to collect the sputum. A markedly inverted position is necessary for effective drainage; it is useless to allow the patient to lean over the side of the bed with his elbows on a chair or to elevate the foot of the bed a few inches. The patient breathes deeply during postural drainage, to encourage prompt evacuation of exudate. Acutely ill or weakened patients may be unable to sustain the exertion of postural drainage by this method; in such cases the bed is placed in Trendelenburg position with eighteen inches of elevation at the foot, and the patient is placed on his side, with the diseased lung uppermost. Postural drainage by inversion usually is effective within several minutes and can be carried out as often as necessary during the day without too much discomfort; drainage by elevation of the foot of the bed requires at least several hours a day. For maximum effect the bed is kept elevated throughout the entire day to promote efficient emptying of the bronchial

exudate. Steam inhalations and expectorant drugs may aid drainage by thinning the exudate; bronchodilating drugs such as epinephrine administered parenterally in small dosage or by nebulizer just before postural drainage also are of value. Occasional bronchoscopic aspiration is advisable in most cases.

When postural drainage is performed properly and faithfully, a marked improvement in general health and in the local pathologic process soon ensues. The patient gains weight and strength, the amount of sputum decreases and the fetid odor diminishes, and the attacks of respiratory tract infection and pneumonitis become less frequent.

**In the Operating Room.**—An infusion of dextrose (5 per cent) in distilled water is begun when the operation is started so that a transfusion can be given without delay if the need arises. Administration of from 500 to 1,500 c. c. of blood is advisable as a routine procedure during or immediately after operations involving resection of pulmonary tissue; transfusions are most effective when blood is replaced as it is being lost rather than at a later time when the effects of hemorrhage have become clinically evident.

When postoperative leakage of blood, air, or exudate is expected, intercostal tube drainage (p. 562) of the chest is instituted at operation to provide for removal of the accumulations of air or fluid during the days immediately following operation. The tubes are clamped tightly at the time of insertion, and the clamps are not removed until after each tube has been connected to a separate waterscal or constant suction apparatus. Any air still trapped in the pleural cavity is removed by aspiration through the anterior intercostal catheter or, if no catheter has been inserted, by anterior thoracentesis. The tracheobronchial tree is cleared of mucus and blood by bronchoscopic aspiration before the patient leaves the operating room. Bronchoscopy is the method of choice but can be performed only if the patient is still anesthetized; if the stage of recovery is beginning, reflexes are appearing, and the mouth and jaws are tight, bronchoscopy is too difficult and tracheobronchial aspiration is performed by catheter suction. In either case an effort is made to clear both bronchi of secretions. Betts and Lees<sup>7</sup> have advised the intravenous administration of atropine, 0.6 mg. (gr. 1/100), before per-

formance of tracheobronchial suction in a partially anesthetized patient to prevent the occurrence of a vagovagal reflex.

**Postoperative Care.**—A private room and special nurses are engaged if possible. The patient is placed in the horizontal or Trendelenburg position until fully conscious in order to promote drainage and prevent shock. The blood pressure and pulse rate should be taken every fifteen minutes for several hours until stabilized. During the early postoperative period, the patient should lie on the operated side to avoid any interference with function of the good lung. While occasional changes to the supine position are permissible, the patient is not allowed to lie with the operated side uppermost during this time; expansion of the intact lung is impaired and secretions from the traumatized lung may drain downward into the other, with resultant bronchial occlusion and possible atelectasis. When recovery from anesthesia is complete and the danger of shock is past, the patient should be propped up to encourage drainage of pleural exudate through the intercostal tubes. Care of the tubes has been outlined on p. 562

Oxygen is supplied as a routine measure for at least twenty-four hours; an intranasal catheter supplying from 5 to 6 liters of oxygen per minute is satisfactory. A face mask of the Boothby, Barach, or Lombard types will supply higher concentrations of oxygen but will be less acceptable to the patient. In no case, however, should a face mask be used until recovery from anesthesia is complete, since the patient may vomit during this time. Oxygen is not often necessary for more than a day or two, although it should be supplied at any time if the patient shows tachycardia, dyspnea, slight cyanosis, or signs of impending shock. Use of oxygen as a therapeutic measure is often delayed too long; it should be supplied when the slightest indication develops rather than when the need for it is plainly apparent.

Deep-breathing exercises are carried out each hour in the presence of an attendant, and exercising movements of the legs and feet are required at frequent intervals. Voluntary coughing is encouraged whenever there is evidence of accumulating bronchial secretions. Most patients will object to these procedures but should be urged firmly to carry them out in spite of the temporary discomfort they cause. Regular changes of position and exercise of the extremities will aid greatly in prophylaxis of



thromboembolic disease, in improvement of circulatory and respiratory function, and in rapid return of strength. Full respiration and voluntary cough are of much value in prevention of atelectasis. If deep breathing is not performed voluntarily, it can be induced by administration of carbon dioxide (100 per cent) through a funnel held several inches from the patient's nose for three or four breaths; more than this is not necessary. When coughing is difficult because of pain in the wound, a single dose of morphine can be given to relieve the discomfort without depressing the respiration; coughing will then be possible if the attendant will support the wound with firm manual pressure. The most effective method of reducing pain on cough, however, is by paravertebral procaine block of the regional intercostal nerves. In occasional cases, clearing of bronchial exudate will be facilitated by placing the bed in Trendelenburg position for a short time. Steam inhalations, with or without medication, are soothing if an unproductive cough is present and may help to loosen the viscid exudate.

When rales are present and cough is not fully effective, suction aspiration of the tracheobronchial tree is carried out without too much delay. Following total or partial pneumonectomy, bronchoscopy is preferable to catheter suction and should be done before rather than after atelectasis develops. An x-ray film is taken following bronchoscopy to insure that no areas of lung still remain blocked by bronchial exudate.

Sedatives are required only occasionally if intercostal nerve block is performed at operation. Both narcotic and hypnotic drugs are used when necessary to relieve pain or induce restful sleep but are given in minimal quantities in order to avoid depression of respiration and of general physical activity. Some of the newer analgesic drugs which produce relief of pain without depression of respiration may prove to be superior to morphine in routine care of patients who have undergone thoracic surgery.

Pulmonary resection is accompanied by significant loss of blood; even though several transfusions have been given before and during operation, administration of additional blood is indicated if recovery from anesthesia is slow, if signs of incipient shock are present, or if the blood pressure remains below normal. Reduction of the alveolar tissue available for oxygen exchange also necessitates maintenance of the blood hemoglobin at as

high a functional level as possible. Hematologic examination may not reveal anemia due to blood loss until several days have passed; blood studies therefore are made at frequent intervals during the postoperative course. Postoperative blood transfusions are given slowly and at intervals to avoid overloading of the pulmonary circulation, with consequent pulmonary edema.

Fluids are supplied in sufficient quantity to meet the daily water requirements; little fluid is needed during the day of operation if moderately large amounts of blood have been transfused. As a rule, one or two infusions (1,000 c.c.) of dextrose (5 per cent) in distilled water will suffice for the twenty-four hour period following operation; amounts of fluid totaling 2,500 c.c. daily by all routes will be adequate thereafter. Normal salt solution is not used for a period of forty-eight hours after operation; the development of salt lack at this time is much less likely than the retention of salt, with pulmonary edema. Moreover, appreciable quantities of salt are supplied by blood and plasma transfusions or by protein hydrolysate infusions given during the immediate postoperative period. The total daily urinary output is measured and the chest is examined frequently by auscultation to insure that the fluid intake is sufficient but not excessive.

Penicillin, begun a day or two before operation, is continued for five days after operation as a prophylaxis against infection. If infection is present or should develop, penicillin is continued as long as necessary and may be supplemented with sulfadiazine. Streptomycin is indicated only in the treatment of infections due to gram-negative bacteria.

Diet is adjusted to the patient's ability to take food. A high protein, high carbohydrate liquid diet is provided as soon as possible; the diet is increased progressively and high protein supplementary feedings are added. Therapeutic doses of vitamin concentrates (B complex and C) are continued.

Following *total pneumonectomy*, the empty pleural space becomes obliterated gradually by shift of the mediastinum toward the defect, compensatory emphysema of the intact lung, elevation of the homolateral leaf of the diaphragm, collection of serofibrinous exudate, thickening of the parietal pleura, and retraction of the chest wall. To reduce the volume of the empty hemithorax still further, some surgeons have advised the performance of

thoracoplasty at a later date, although this procedure is being used less than in the past.

X-ray and fluoroscopic examinations of the chest are made at intervals of two to three days to follow the progress of post-pneumonectomy healing and to detect excessive accumulations of air or fluid. Large collections of air or exudate are removed by thoracentesis as often as necessary, although aspiration should be stopped if the patient complains of tightness or pain. A negative pressure strong enough to cause mediastinal shift and sudden overdistention of the remaining lung is undesirable; the intrathoracic pressure should be adjusted to maintain the mediastinum in its normal position for at least several days after operation. Accumulations of fluid and air that do not displace the mediastinum are allowed to remain; the air is soon absorbed spontaneously and the fluid gradually thickens to a gelatinous consistency, with formation of a heavy fibrinous layer on the pleural surface. The incision is usually closed without drainage at operation; if intercostal catheter-waterseal drainage is instituted for some reason, however, suction is not applied for several days unless necessary to maintain the mediastinal structures in their normal mid-position. After this length of time, gentle suction ( $-8$  to  $-10$  cm. of water) can be applied to draw the mediastinum gradually toward the empty hemithorax.

While collection of sterile exudate in the empty pleural space favors obliteration of the cavity, it also presents a potential hazard in the occasional case in which bronchopleural fistula develops. Opening of the bronchial stump following pneumonectomy carries an extremely high mortality rate, few patients surviving this complication. Symptoms include cough, dyspnea, and evidences of tension pneumothorax; in some cases an abundant discharge of serous or sero-hemorrhagic fluid is coughed up from the trachea. If the stump opens widely, pleural serous exudate may be sucked rapidly through the opening, with flooding of the bronchial tree in the opposite lung. In other cases, sudden development of pneumothorax may cause marked reduction of vital capacity due to displacement of the mediastinum and interference with function of the intact lung. Whether the bronchial leak is large or small, empyema will develop subsequently as a result of passage of bacteria through the open bronchus into the pleural cavity filled with serofibrinous

fluid. Immediate treatment includes bronchoscopic aspiration if necessary, prompt establishment of constant suction drainage (-8 to -12 cm. of water) through anterior and posterior intercostal tubes, administration of oxygen by nasal catheter or mask, and administration of penicillin in high dosage. Intercostal drainage is continued until the bronchopleural fistula is entirely healed, which may require three or more weeks. Empyema developing in these cases is treated in the usual manner by aspiration of collections of thin pus not sufficiently drained by the intercostal tube and by open drainage with rib resection after several weeks have passed and the bronchopleural fistula is solidly healed. Multiple pleural abscesses may occur, necessitating resection of the overlying rib segments for external drainage; thoracoplasty will be necessary later to obliterate the chronic empyema pockets in such a case.

Chief causes of death following pneumonectomy include cardiovascular complications, pulmonary embolism, pneumonia, opening of the bronchial stump with empyema and pneumothorax, hemorrhage, and postoperative shock. Total pneumonectomy for carcinoma still presents a discouraging picture; Ochsner and associates<sup>13</sup> report statistics of their clinical cases which show that resection will prove to be possible in scarcely more than one-third of the patients, and of this small group approximately one-fourth of the patients succumb to operation and only about one-fifth survive for five years. The operation is distinctly worth while in spite of the low survival rate, however, since the mortality of untreated pulmonary malignancy is 100 per cent.

Following *lobectomy*, the chief consideration is the prompt re-expansion of the remaining lung tissue. In some cases the amount of exudation following lobectomy is slight and of little significance; in other cases, a large amount of serous fluid may collect, for example, when pleural adhesions must be freed, or hilar inflammation is present, or contamination occurs during operation, or the tourniquet technique must be used for hilar ligation. Accumulation of fluid following lobectomy will prevent full re-expansion of the lung and will favor development of empyema; postoperative catheter drainage therefore is employed.

Each intercostal drainage tube is connected to a separate waterseal or constant suction drainage apparatus (Figs. 61 and 62).<sup>16</sup> Although pulmonary re-expansion should be complete within twenty-four to forty-eight hours, it is not advisable to apply suction exceeding  $-8$  to  $-10$  cm. ( $-3$  to  $-4$  inches) of water; excessive reduction of intrathoracic pressure will cause pain in the chest and will encourage oozing of blood from the field of operation.

Strong negative pressure in the chest at this stage also tends to pull accumulations of mucus deeper into the bronchi and to decrease the efficiency of coughing. Close watch is kept to make sure that the tubes function properly and that the chest remains clear; if air or fluid accumulates in spite of the catheter drainage, thoracentesis is done at once and repeated as necessary. Following thoracentesis on each occasion, penicillin (100,000 units in 20 c.c. of sterile normal salt solution) is instilled into the chest. Sampson and Collis<sup>17</sup> have suggested that postlobectomy atelectasis accompanied by pleural effusion should be treated by bronchoscopy before the effusion is tapped; if the fluid is withdrawn first, the increasing negative intrathoracic pressure will cause mucus to be drawn deeper into the small bronchi.

If re-expansion is not complete after two days have passed, even though the pleural accumulations of fluid and air have been removed, bronchoscopic aspiration is performed to eliminate atelectasis as a possible cause. The amount of catheter suction can be increased gradually and progressively up to  $-8$  to  $-12$  inches of water after this time if necessary. Care of the intercostal catheters has been described (p. 562).

Prompt expansion of the remaining lung is usually followed by rapid recovery; if re-expansion is delayed, such serious complications as atelectasis, bronchopleural fistula, and massive empyema may ensue. Atelectasis in the remaining lobe often leads to consolidation and pneumonitis, with delay in convalescence. Prompt re-expansion of the remaining lobe also tends to reduce the incidence of bronchopleural fistula and empyema both by filling the thoracic cavity completely and by covering the freshly cut bronchial stump. Leakage of air or local abscess formation around the sutured bronchus then tends to remain limited to a small area in the mediastinum, and sub-

sequent healing and absorption of exudate is more likely to occur spontaneously.

An anterior catheter, if used, is withdrawn as soon as air is cleared from the intrapleural space. A posterior tube, however, is allowed to remain for ten to fourteen days to keep the chest cleared of exudate until firm adhesions have formed between the expanding lung and the parietal pleura; too early removal of the catheter may permit exudate to accumulate and the lung to be collapsed away from the thoracic wall. Occasionally a small empyema pocket will develop at the lung base, requiring treatment by rib resection and closed suction drainage approximately three to four weeks after operation.

### **Pulmonary Resection for Suppurative Disease.—**

**BRONCHIECTASIS.**—Unusually good results are obtained in selected cases by removal of the diseased portions of the lung in treatment of bronchiectasis. The mortality of the procedure has steadily declined almost to a negligible figure with improvements in surgical technique and in hospital care of the affected patients; the report of Kay and associates,<sup>18</sup> describing 220 consecutive lobectomies for bronchiectasis with a single postoperative death, is typical of the excellent results being obtained in many medical centers.

Less than half of patients with bronchiectasis are eligible for surgery, however; operation is most successful in young people who have had the disease only a short time and in patients with involvement of only one lobe. If suppurative disease of the bronchi has been present over a period of years, particularly if onset was at an early age, prolonged atelectasis and infection of the surrounding lung tissue will be present, with fibrosis and destruction of the involved pulmonary parenchyma; empyema also may occasionally develop in such cases. Patients of this type are likely to be poor operative risks; postoperative pulmonary re-expansion tends to be slow, with resulting anoxia and cyanosis, and pneumonitis and empyema are likely to complicate recovery. Patients with asthma, cardiovascular disease, or chronic emphysema also are poor risks for lobectomy because of the dangerous reduction in vital capacity. While operation is safest in patients with unilateral bronchiectasis, it is pos-

sible in some cases with bilateral disease to resect the involved lobe or lobes of the right lung at one stage and the left lower lobe and lingula several months later. A procedure of this extent can be done only if the patient is an excellent operative risk and if there is no evidence of disease in either upper lobe (with the exception of the lingula); these two lobes must be sufficient to carry on the respiratory requirements following operation. The postoperative course in patients with bilateral bronchiectatic disease is a great deal more likely to be complicated than in those in whom all the involved lung tissue can be removed at a single stage.

Preoperative preparation, as outlined previously, is designed to improve the patient's general condition, to decrease the amount and rate of production of sputum, and to reduce the residual inflammation around the diseased bronchi. Bronchographic studies are made to outline the bronchial tree in each of the five lobes, roentgenograms being obtained in postero-anterior, lateral, and right and left oblique planes. X-ray visualization is repeated if necessary until fully satisfactory demonstrations are made throughout both lungs. Operation is not performed until all the iodized oil has been cleared from the lungs, which usually requires two months or more. During this period of delay, an appropriate diet is taken, with supplementary protein feedings, iron preparations, and vitamins; postural drainage is performed for as long a period each day as possible, with bronchoscopic aspiration at intervals; and moderate exercise is advised.

Operation is planned when the patient's general condition has improved sufficiently, the foul odor of the sputum has cleared, and the amount of sputum has decreased to a minimum; if empyema has been present, it should be cured completely before operation is undertaken. While not entirely necessary, it is best to perform lobectomy for bronchiectasis in the summer months when the incidence of respiratory tract infection is lowest.

The patient should enter the hospital at least two weeks before operation. Laboratory studies are made, measures for improvement of the general condition are undertaken, postural drainage is continued, vital capacity is determined, and thorough examination of the sputum is made, including acid-fast stains.

Bronchoscopy is performed during this time to note the degree of progress since initiation of treatment as well as the amount of acute inflammation remaining in the affected areas. Penicillin is administered intramuscularly to control the peribronchial inflammation and pneumonitis and by aerosol to reduce the bronchial suppuration and formation of sputum. Doses of 50,000 units in aqueous solution every three hours are given by intramuscular injection for a week before and a week after operation. Aerosol penicillin inhalation is of considerable value in reducing the acute inflammation of the bronchial mucosa; within ten to fourteen days the sputum becomes thinner, less purulent, of a less offensive odor, and decreased in amount. Improvement due to aerosol penicillin is measured by recording the amount and character of the sputum recovered each day, with occasional bacteriologic examination; penicillin is continued until secretion is minimal. Longer periods of treatment are required for patients with long-standing disease, especially if saccular dilations, abscess cavities, or areas of atelectasis are present. To be of value, aerosol penicillin must be used in conjunction with postural drainage; the medication cannot pass through bronchi blocked by accumulations of thick mucus.

Aerosol penicillin can be given with little difficulty by the technique recommended by Findlay and Sweet,<sup>19</sup> using a Vaponephrin nebulizer connected to an oxygen tank by means of a rubber tube equipped with a Y tube. Penicillin (50,000 units in 1 c.c. of normal salt solution) is placed in the nebulizer and oxygen flow is set at 5 liters per minute. Inspiration should be deep and slow, and each breath is retained for five seconds before exhalation. The open arm of the Y tube is blocked only during actual inhalation and is allowed to remain open during expiration and while the patient holds his breath. The oxygen current therefore flows through the nebulizer only during inspiration, penicillin being vaporized only at this time. Aerosol penicillin is given every three hours during the day and night, twenty minutes being required for each dose; as improvement proceeds, one night dose can be omitted. The nebulizer is cleaned with normal salt solution after each dose of penicillin.

Operation is best performed in the early afternoon to permit preoperative postural drainage and evacuation of the night sputum. Because of the presence of inflammatory changes, the



operation must be done with care; lobectomy for inflammatory disease may be more difficult than total pneumonectomy. Post-operative care is directed toward prevention of shock and anoxia, promotion of rapid re-expansion of remaining lung tissue, and prevention or prompt withdrawal of pleural accumulations of fluid and air. Transfusion of blood and administration of oxygen in high concentration is routine in all cases. Atelectasis or failure of expansion of the remaining lung tissue is one of the commonest serious complications; every effort is made to keep the bronchi free of accumulating mucus and to keep the pleural cavity free of accumulating air, exudate, or blood. Care of the drainage tubes has been outlined previously (p. 562).

**LUNG ABSCESS.**—The pathologic process characteristic of lung abscess progresses rapidly through its early stages, an area of necrosis with surrounding suppurative pneumonitis developing within a few days. As the gangrenous pulmonary tissue liquefies, a cavity is formed, usually with erosion into a bronchus and spontaneous evacuation. Completely drained lung abscess cavities will heal; if drainage through the bronchus is adequate, a cure can be effected occasionally in favorable cases by medical supportive treatment. As a rule, however, bronchial drainage does not keep the cavity sufficiently empty to permit total collapse of its walls and obliteration. With progression to the chronic stage after six weeks or more, scar tissue develops in the abscess wall, which becomes rigid and resistant to collapse.

Preliminary treatment of early acute lung abscess includes general care of the usual type with high protein diet, vitamins, penicillin, and blood transfusion as indicated, postural drainage for as prolonged periods as possible, bronchoscopy at intervals, and complete bed rest. Bronchoscopy is performed both for identification of the bronchus through which the pus is draining and for evacuation of the abscess cavity; occasionally a foreign body is found and can be removed. The patient should remain in bed with the involved side downward, particularly when asleep, to avoid flow of pus into the bronchial tree of the intact lung. Artificial pneumothorax is never used for collapse therapy of a cavitation due to putrid lung abscess; it is dangerous in the early stages because spread of the necrotizing pneumonitis may result from increase in intrathoracic pressure and in any case it may cause tearing of pleural adhesions with resultant empyema.

Aspiration by a thoracentesis needle is never permissible in diagnosis or treatment of lung abscess; pus will be deposited along the track of the needle during withdrawal, with resulting empyema or spread of infection within the pulmonary parenchyma.

Acute lung abscess is treated conservatively for two to four weeks following onset; spontaneous healing will be evident by this time in favorable cases. Surgical drainage by pneumotomy is performed within three to six weeks after onset if symptoms are progressive and the patient's condition shows no improvement. If operation is delayed until more than two months have passed, the disease will have progressed into the chronic stage, with deterioration in the patient's general health and deposition of rigid scar tissue in the wall of the abscess. As originally demonstrated by Neuhof and Touroff,<sup>29</sup> surgical drainage of putrid lung abscess within the first several weeks of the disease will produce a much higher percentage of cures and a much lower incidence of serious complications than will delay of drainage until the stage of chronicity, after a prolonged trial of non-surgical treatment. These authors emphasize the facts that the abscess is fully developed within two weeks, with a well-demarcated cavity and liquefied contents, and that adhesions between the overlying lung and the chest wall are almost invariably present by this time. If the abscess is allowed to progress to chronicity under supportive treatment, spreading pneumonitis is likely to occur, with production of multiple abscesses, atelectasis, pulmonary fibrosis, bronchiectasis, or empyema with formation of localized pockets. In such cases surgical drainage affords a variable degree of improvement but rarely effects a cure; residual sinuses, bronchocutaneous fistulas, and evidences of undrained infection may remain after operation. The patient's general condition progressively deteriorates and metastatic abscesses may occur, life expectancy being relatively short when residual infection persists.

Practically all lung abscesses lie distally in the pulmonary parenchyma beneath the pleural surface and in close proximity to the thoracic wall, the overlying layer of lung tissue being thin, airless, and avascular. In some cases, however, the lesion approaches the pleural surface opposite the diaphragm, the mediastinum, or the interlobar fissures rather than opposite the costal pleura, this type being somewhat inaccurately termed

"central abscess." While external surgical drainage of lung abscesses is facilitated by their peripheral location, accurate identification of the involved bronchopulmonary segment and exact localization with reference to the chest wall are necessary before surgery can be undertaken.

For localization of the lesion, roentgenograms are made in the posteroanterior, lateral, and oblique planes. If the site of the abscess is uncertain or the patient is acutely ill, Neuhof<sup>21</sup> advocates use of the "spot" method of localization suggested by Rabin. According to this procedure, the relation of the abscess to the chest wall is determined as exactly as possible by fluoroscopic or x-ray study, and a small amount of a sterile mixture of iodized oil and methylene blue is injected into the intercostal musculature at this point. X-ray films are then taken to demonstrate the relation of the iodized oil to the abscess; the oil may be immediately over the lesion or as much as several centimeters distant. At operation the methylene blue is exposed, giving a fixed point of reference to the abscess and permitting accurate operative exposure. To avoid error the iodized oil must be injected into the intercostal muscle rather than into the subcutaneous tissue.

Measures similar to those used in conservative treatment are continued until the patient is in satisfactory condition. Operation is performed under general anesthesia, a segment of rib being excised as exactly as possible over the site of the lesion. The overlying parietal pleura should be found to be thickened and opaque. An aspirating needle is inserted through the adherent pleura to identify the abscess cavity, which is then unroofed with the actual cautery. Pockets are broken down very gently by insertion of the finger, and a fine-meshed gauze pack is introduced. The procedure usually followed when pleural adhesions are absent is to pack the wound with gauze down to the intact pleura and apply a dressing; five to six days later, when pleural adhesions have developed in response to the irritation of a foreign body, the pack can be removed and the abscess drained without danger of empyema.

Postoperative improvement should be prompt and progressive, if not, it is probable that undrained pockets are still present. The pack is removed and changed under general anesthesia (sodium pentothal) after five to six days and is changed every

three to five days as necessary thereafter. The resulting wound is allowed to heal slowly by granulation from the bottom, over a period of four to eight weeks, to insure complete eradication of the anaerobic organisms. The opening in the chest wall is kept open by means of a pack or soft rubber tube until the patient is entirely free of symptoms, sputum has disappeared, and x-ray shows no evidence of pulmonary infiltration.

Complications following pneumotomy sometimes are serious; sudden emptying of the abscess into a bronchus during operation may fill the trachea with putrid pus and flood the bronchial tree of the intact lung. Hemorrhage may occur after operation from a blood vessel in the abscess cavity, eroded by the gangrenous pneumonitis, although presence of the pack tends to minimize this danger. Persistent bronchial fistula, with external leakage of air through the wound, is a frequent complication of surgical drainage for chronic lung abscess and occasionally may cause a significant reduction in vital capacity. Bronchopleurocutaneous fistulas usually heal spontaneously but may prove resistant to conservative measures, requiring later operative repair or lobectomy.

Because external drainage is only partially effective in treatment of chronic lung abscess, lobectomy is being employed in an increasing number of selected cases. Sweet<sup>22</sup> has abandoned many of the secondary operations for treatment of chronic abscess, such as thoracoplasty, plastic procedures for closure of chronic cavities, and even redrainage after failure of primary surgical drainage; he advocates early surgical drainage during the first few weeks, with lobectomy if pneumotomy fails to cure or if the patient is first seen in the chronic stage, with an advanced abscess or a history of significant hemorrhage. Valle<sup>23</sup> recommends lobectomy if the cavity does not heal and bronchopleural fistula persists for as long as six months following cautery drainage, cautioning that lobectomy should not be done while the infection is still active. Lindskog<sup>24</sup> advises primary resection, without preliminary surgical drainage, for chronic abscess with multiple pockets or widespread destruction in one or more lobes, secondary bronchiectasis, atelectasis and pneumonitis not improved by bronchoscopy, severe bleeding, or perforation with loculated empyema. While the mortality rate of lobectomy for pulmonary abscess is still high, it is lower than that of in-

effective conservative treatment, and the operation will produce permanent cure in properly selected cases.

Patients with lung abscess are prepared for lobectomy in much the same way as patients with bronchiectasis; it is particularly important to reduce local inflammation by properly performed postural drainage, with bronchoscopy at intervals. High protein diet, supplementary high protein feedings, large doses of vitamin preparations, and administration of blood transfusions until the patient's hemoglobin, hematocrit, and blood volume reach normal levels are indispensable preoperative measures; penicillin is administered by aerosol and by intramuscular injection as in the patient with bronchiectasis. The cavity is emptied by postural drainage on the morning of operation and bronchoscopy is done after anesthesia has been induced. An infusion is started before the incision is made so that blood can be administered later without delay; as a rule, from 500 to 1,500 c.c. of blood are given during lobectomy. It is well also for the anesthetist to be prepared for bronchoscopy during the course of operation in the event that the abscess should suddenly discharge its contents into the trachea. Lobectomy is especially difficult in these cases because of pronounced inflammatory infiltration and induration of the hilar structures and lymph nodes.

Empyema will occur in a very high percentage of cases following lobectomy for lung abscess, especially if the tourniquet technique is used or if the operation is secondary to a previous drainage procedure. For this reason drainage of the chest by intercostal catheter may be insufficient; a small segment is resected from the eighth rib in the posterior axillary line and a soft rubber tube (one-fourth inch) is inserted to fit snugly into the pleural opening and is fixed to the chest by an airtight dressing. If contamination has occurred during operation or if postoperative empyema is reasonably certain to develop, a short segment of the sixth rib also is resected in the mammillary line and a similar rubber tube inserted. Each tube is connected to a waterseal apparatus for closed drainage.

Postoperative care and management of the drainage tubes are the same as following lobectomy for other conditions. Blood transfusions are necessary even though the blood constituents were close to normal before operation and transfusions were

given in the operating room; penicillin is administered routinely for several days before operation and for at least seven days afterward. Serious complications, besides those to be anticipated following any lobectomy, include rapidly developing sepsis with spreading pneumonitis, empyema with residual abscesses, and subphrenic space infection.

**Pulmonary Tuberculosis.**—Perhaps the cardinal principle in the treatment of pulmonary tuberculosis is the institution of absolute rest both for the diseased lung and for the patient. Progressively improved methods of attaining this objective have produced correspondingly improved therapeutic results. Sanatorium care with absolute bed rest, nutritional therapy, and an attitude of optimism and encouragement are fundamental measures of securing psychic and physical rest for the patient; various methods of collapse therapy are employed to secure physiologic rest for the diseased tissues.

Progress of the tuberculous lesion depends upon the relation between exudative tissue destruction and reparative healing fibrosis; necrosis of tissue is followed by liquefaction and cavitation, which is the most serious deterrent to healing and the chief cause of chronicity in pulmonary tuberculosis. As in the case of putrid lung abscess, spontaneous drainage is effected through a communicating bronchus. Tuberculous cavities, however, usually drain completely but have little tendency to heal spontaneously, while lung abscesses rarely drain completely but will usually heal if they do.

Persistence of the tuberculous cavity is due to progressive excavation and continued exudative infiltration in some cases and to rigid organization of the walls with chronic scarring and deposition of fibrous tissue in others. When optimum conditions are present, small cavities with complete drainage sometimes will heal by scarring. In other cases, effective contraction of the lesion will be prevented by pathologic changes in the surrounding lung and pleura. For example, fibrous organization in the parenchyma around the lesion will splint the walls of the cavity and prevent contraction; inflammatory adhesions between the overlying parietal and visceral pleural surfaces will exert traction on the subjacent cavity wall and tend to hold it open; and progressive pulmonary parenchymal fibrosis will

reduce the healing power and the resistance to infection of the lung tissue itself. In addition, the alternating tension and relaxation produced by the respiratory movements of the thorax and diaphragm keep the diseased tissue in a state of constant activity that interferes greatly with the progress of repair. An open cavity acts as an ever-present source of tuberculous infection, predisposing to spread of the disease to other parts of the lung, to the tracheobronchial tree, to the opposite lung, or to the blood stream, with metastasis throughout the body. Hemorrhage may take place from eroded blood vessels within the cavity wall, secondary infection of the cavity with pyogenic organisms may occur, or tuberculous or mixed empyema may develop, in some cases with a complicating bronchopleural fistula.

Frequent x-ray examinations of the chest are made in the patient with early tuberculosis to follow the progress of the disease and to detect the first evidence of cavity formation; active measures to promote healing are undertaken as soon as such a lesion is noted. Treatment by collapse therapy is being instituted earlier in the course of the disease than formerly, with considerable improvement in results. Serial roentgenograms of the chest are of the greatest importance in evaluating the course of the disease and, to afford maximum information, should be studied with the help of a radiologist. Throughout his entire illness, the patient with cavitation due to pulmonary tuberculosis should be cared for by the internist working in close cooperation with the surgeon. Successful surgical treatment of pulmonary tuberculosis requires considerable experience with every aspect of the disease; proper choice and accurate timing of the operative procedures are possible only by consideration of the individual patient from both the medical and the surgical standpoints.

Tuberculous pulmonary lesions which do not respond to more conservative methods of collapse therapy are treated by *thoracoplasty*, which permits selective permanent collapse of the diseased area of lung, with preservation of function of normal lung tissue. The upper part of the lung can be collapsed more effectively by this means than by any other. Resection of graduated lengths of from five to eight ribs is necessary to secure full relaxation and immobilization of the involved lung area; the pro-

cedure is performed in stages approximately three weeks apart, not more than three ribs being removed on each occasion.

Thoracoplasty is a serious operation, the mortality rate ranging up to 10 per cent, and both the deformity caused by removal of part of the bony thoracic framework and the de-functionalization of the underlying lung are permanent. Improved general care and earlier employment of the operation, however, are beginning to effect a sharp reduction in mortality rate, with corresponding improvement in operative results. Patients to be treated by thoracoplasty are chosen with care and their entire preoperative and postoperative courses are followed by the internist as well as the surgeon. The chief indications for thoracoplasty in tuberculosis include fairly extensive unilateral disease, particularly in the upper lung region, with or without cavitation but with evidence of fibrosis and a healing reaction and with little or no response to collapse therapy by artificial pneumothorax. Chronic nontuberculous pyogenic or mixed empyema which cannot be controlled by rib resection and open drainage also may be treated satisfactorily by thoracoplasty as a final resort. Thoracoplasty is not applicable to patients who are poor surgical risks; some of the contraindications to the operation include actively progressing tuberculous lesions in either lung, particularly at the base, or in other parts of the body, and associated disease such as asthma, emphysema, heart disease with impairment of cardiac function, renal or hepatic disease, or diabetes.

Before operation is planned, complete blood studies are obtained, including red and white cell counts, hemoglobin content, hematocrit, and serum protein concentration; transfusions are administered until the blood values have reached fully normal levels. Liver and kidney function studies also are made. The vital capacity is determined, patients who exhibit a vital capacity below 1,200 c.c. are not acceptable surgical risks in general. If evidences of cardiac disease are present, the necessary studies are performed, although the most dependable information can be obtained by such simple functional tests as determination of exercise tolerance and the ability of the patient to hold his breath. Reduction of vital capacity and of exercise tolerance sometimes may be due simply to poor muscle tonus in patients



who have been confined to bed; considerable improvement can be secured by permitting graded amounts of exercise before operation. In other respects general preoperative measures are much the same as those instituted before any other major operation.

The greatest immediate danger of thoracoplasty is the production of shock in a weakened patient. Although the procedure should not be prolonged, every effort is made to operate with gentleness, to avoid loss of blood, and to secure perfect hemostasis. Transfusion is given during operation in all cases and after operation as a routine; oxygen also is of value during the early postoperative period. Further depression of an already diminished cardiac reserve may occur following removal of several ribs because of mediastinal shift and reduced pulmonary ventilation; sagging of the left anterior chest wall against the heart is prevented by allowing several centimeters of the anterior rib ends to remain.

In some cases *paradoxical respiration* will be noted; resection of large segments of several adjacent ribs reduces thoracic support so that the affected portion of the chest wall will be drawn inward on inspiration and forced outward on expiration. The paradoxical movements reduce the efficiency of respiration and interfere with air exchange in the normal lung tissue. Dyspnea, anoxemia, and interference with cardiac function are produced. Moreover, loss of support in the overlying chest wall reduces the effectiveness of cough in clearing secretions from the collapsed lung and even permits air to be blown into the relaxed lung during cough, forcing the accumulated secretions deeper into the bronchi. Collecting secretions tend to overflow from the collapsed lung downward into the uninvolved lung, and atelectasis and pneumonitis may result. Paradoxical respiration can be diminished and its untoward effects prevented by preoperative and postoperative aspiration of any air or fluid that has accumulated in the pleural cavity and by firm pressure strapping over the area of rib resection.

General measures of postoperative care are instituted, including frequent changes of position, exercise of the arms and legs, deep breathing and prophylactic coughing to keep the tracheobronchial tree clear, and maintenance of an adequate fluid and nutritional intake. Wound infection is not uncommon

following thoracoplasty; the character of the incision and of the operative procedure itself tend to favor the growth of contaminating bacteria. When significant infection develops, administration of penicillin is begun at once and enough sutures are removed promptly to afford ample drainage for the entire involved region. If adherent pleura or diseased lung is torn during operation, especially in the vertebral region, tuberculous wound infection or empyema may result.

The patient's cardiorespiratory equilibrium and general physical condition return to a satisfactory state within three to four weeks following thoracoplasty, and the next stage can be performed. Following the second stage, so much support has been removed from the chest wall that adhesive strapping is insufficient and a broad binder is required. A pressure dressing is used after thoracoplasty not only to prevent paradoxical respiration, but also to increase the degree of collapse of the chest wall and to maintain compression of the collapsed lung until sufficient bony growth from the remaining periosteum has taken place to fix the thoracic wall permanently in its new position. Gauze pads or rubber sponges may be used, although many operators have devised thoracoplasty binders according to their own preferences. Skinner<sup>25</sup> suggests the use of a sponge rubber ball wrapped in Kleenex, pushed firmly into the site of the thoracoplasty, and held in place by broad adhesive tape straps, applied tightly in a circular fashion; the chest is protected by stockinet.

*Resection of the lung* is being employed with increasing frequency in treatment of patients with tuberculous lesions who do not respond to artificial pneumothorax or to thoracoplasty. Since tuberculosis, unlike early carcinoma or bronchiectasis, cannot be eradicated by pulmonary resection, the selection of patients for treatment by this method requires a considerable amount of judgment and experience from both the medical and the surgical aspects.

According to present indications,<sup>26</sup> pulmonary resection is most useful in treatment of tuberculous bronchial stenosis with irreparable damage to the lung behind the point of obstruction or of rigid thick-walled cavities that cannot be treated effectively by prolonged artificial pneumothorax or thoracoplasty. Other indications that are less clearly defined include the presence of

relatively advanced degrees of tuberculous atelectasis or bronchiectasis or of large areas of well-demarcated tissue destruction, with no active lesions elsewhere in the pulmonary parenchyma. The mortality rate for pulmonary resection in tuberculosis has decreased greatly as a result of careful evaluation and proper selection of cases and of unremitting care during the period of operation. Sweet has emphasized<sup>26</sup> the fact that tuberculous pulmonary disease still remains after resection of the largest or most active foci and that the patient's immunologic forces must be depended upon to overcome the remainder. The operation is not a substitute for collapse therapy, therefore, and is not used if there is a possibility of controlling the disease by artificial pneumothorax or by thoracoplasty. It is especially dangerous when active tuberculous foci, no matter how small, are present in other parts of the lung.

Before operation can be planned, thorough studies of the involved and the uninvolved lung tissues must be made and the condition of the patient investigated from every standpoint, with close collaboration between surgeon and internist. Bronchoscopic examination is performed to search for tuberculous involvement of the bronchi; the level of resection or the possibility of resection is determined in part by the presence of tuberculous ulceration in the draining bronchus, which must be divided at operation through a healthy area uninvolved by disease. Even though preoperative appraisal is made carefully and accurately, however, the extent of disease found at operation may be much greater than expected, and resection may be entirely impossible or pneumonectomy rather than lobectomy may be necessary.

At operation, transfusion of blood is begun as the operation is started. Since the procedure may be difficult and prolonged, at least 1,500 c.c. of blood should be available for administration in the operating room. Following pneumonectomy, the chest is closed without drainage; following lobectomy, intercostal tube drainage may or may not be employed according to the preference of the surgeon. If drainage is not used,<sup>27</sup> residual air or collections of fluid are removed from the chest by thoracentesis sufficiently often to maintain negative pressure and to encourage re-expansion of the remaining lung. Most surgeons drain the chest following lobectomy; Overholt and associates<sup>28</sup>

employ two rubber catheters (24 French) for drainage during the period of twenty-four to forty-eight hours following lobectomy, the tubes being brought through the anterior end of the thoracotomy incision and connected to a suction apparatus supplying negative pressure of about 12 cm. of water. A pressure dressing is applied to the wound and tracheobronchial aspiration is done to clear both lungs of retained secretions.

Postoperative care is generally the same as that following pulmonary resection for other disease, although prolonged complete bed rest and sanatorium care are necessary for a minimum of six months to encourage healing of remaining lesions. Routine performance of surgical collapse therapy is advocated<sup>28</sup> following postoperative recovery from pulmonary resection for tuberculosis, to prevent overdistention of the remaining lung and reactivation of small tuberculous foci. Two-stage thoracoplasty is advised following pneumonectomy and single-stage thoracoplasty is advised following upper lobe resection, in each case leaving the first rib and the transverse processes intact to secure a moderate degree of collapse without production of deformity. Phrenic nerve avulsion is performed without thoracoplasty following lower lobe resection for tuberculosis.

In addition to the postoperative complications common to pulmonary resection for other types of disease, pneumonectomy or lobectomy for tuberculosis may be followed by activation of previously quiescent foci in the remaining lung tissue, by spread of the disease to previously uninvolved areas, or by pyogenic or tuberculous infection of the pleural cavity or of the operative wound.

### References

1. Graham, E. A., Singer, J. J., and Ballou, H. C.: *Surgical Diseases of the Chest*, Philadelphia, 1935, Lea & Febiger.
2. Poth, E. J., and Mathes, M. E.: The Treatment of Acute Empyema by Continuous Tidal Irrigation, *Surgery* 11: 617, 1943
3. Wangenstein, O. H.: Observations on the Treatment of Empyema With Special Reference to Drainage and Expansion of the Lung, *J. Thoracic Surg.* 4: 399, 1935.
4. Ehler, A. A.: Non-Tuberculous Thoracic Empyema. A Collective Review of the Literature From 1934 to 1939, *Internat. Abstr. Surg.* 72: 17, 1941; in *Surg., Gynec. & Obst.*, Jan. 1941.

5. Blades, B., Hamilton, J. E., and Dugan, D. J.: Observations on the Treatment of Empyema Thoracis With Penicillin, *Surgery*, 17: 372, 1945.
6. Sanger, P. W.: Decortication in Acute Empyema Thoracis, *Surg., Gynec. & Obst.* 82: 71, 1946.
7. Betts, R. H., and Lees, W. M.: Military Thoracic Surgery in the Forward Area, *J. Thoracic Surg.* 15: 46, 1916.
8. Brewer, L. A., Burbank, B., Samson, P. C., and Schiff, C. A.: The "Wet Lung" in War Casualties, *Ann. Surg.* 123: 343, 1946.
9. Samson, P. C., Burford, T. H., Brewer, L. A., and Burbank, B.: The Management of War Wounds of the Chest in a Base Center, *J. Thoracic Surg.* 15: 1, 1946.
10. Alexander, J.: Preoperative and Postoperative Care of Patients With Surgical Diseases of the Chest, *Arch. Surg.* 40: 1133, 1940.
11. Blades, B., and Mousel, L. H.: Bronchoscopy and the Surgeon, *S. Clin. North America* 25: 1938, 1945.
12. Rienhoff, W. F., Jr.: The Present Status of the Surgical Treatment of Carcinoma of the Lung, *Ann. Surg.* 125: 541, 1947.
13. Woolner, L. B., and McDonald, J. R.: Bronchogenic Carcinoma: Diagnosis by Microscopic Examination of Sputum and Bronchial Secretions; Preliminary Report, *Proc. Staff Meet., Mayo Clin.* 22: 369, 1947.
14. Graham, E. A.: Indications for Total Pneumonectomy, *Dis. of Chest* 10: 87, 1944.
15. Ochsner, A., DeBakey, M. E., and Dixon, L.: Primary Pulmonary Malignancy Treated by Resection, *Ann. Surg.* 123: 522, 1947.
16. Adams, W. E.: Recent Progress in the Surgical Treatment of Lung Tumors, *Surgery* 10: 1005, 1941.
17. Sampson, H. H., and Collis, J. L.: Postlobectomy Lobar Collapse, *J. Thoracic Surg.* 13: 435, 1944.
18. Kay, E. B., Meade, R. H., Jr., and Hughes, F. A., Jr.: Surgical Treatment of Bronchiectasis, *Ann. Int. Med.* 26: 1, 1947.
19. Findlay, C. W., Jr., and Sweet, R. H.: Aerosol Penicillin as a Therapeutic Adjunct in the Preparation of Patients With Suppuration of the Lung for Pulmonary Resection, *J. Thoracic Surg.* 16: 81, 1947.
20. Neuhof, H., and Touroff, A. S. W.: Acute Putrid Abscess of the Lung; Principles of Operative Treatment, *Surg., Gynec. & Obst.* 63: 353, 1936.
21. Neuhof, H.: Acute Putrid Abscess of the Lung, *Surg., Gynec. & Obst.* 80: 351, 1945.
22. Sweet, R. H.: An Analysis of the Massachusetts General Hospital Cases of Lung Abscess From 1938 Through 1942, *Surg., Gynec. & Obst.* 80: 568, 1945.
23. Valle, A. R.: Lung Abscess, *Surg., Gynec. & Obst.* 81: 278, 1945.
24. Lindskog, G. E.: The Surgical Treatment of Chronic Pulmonary Abscess, *Surgery* 15: 783, 1944.

25. Skinner, E. F.: A Thoracoplasty Binder, *J. Thoracic Surg.* 11: 171, 1945.
26. Sweet, R. H.: Lobectomy and Pneumonectomy in the Treatment of Pulmonary Tuberculosis, *J. Thoracic Surg.*, 15: 373, 1946
27. Churchill, E. D., and Klopstock, R.: Lobectomy for Pulmonary Tuberculosis, *Ann Surg.* 117: 64, 1943.
28. Overholt, R. H., Langer, L., Szyplulski, J. T., and Wilson, J. J.: Pulmonary Resection in the Treatment of Tuberculosis, *J. Thoracic Surg.* 15: 384, 1946.

## CHAPTER 18

### STOMACH

Most patients with gastric or duodenal ulcer do well under medical treatment; healing of the ulcer, relief of symptoms, and restoration of health usually follow proper observance of a well-planned diet, with medication as indicated. A variable percentage of patients, however, either prove refractory to such therapy or develop serious complications; others are unable or unwilling to follow the prescribed routine and show steady increase in pain and progression in symptoms. Because peptic ulcer is a chronic disease that interferes over a long period of time with the intake of sufficient quantities of food and of a properly balanced diet, it is likely to produce significant disability and deterioration in general health, particularly in the 10 to 20 per cent of patients who eventually require surgical treatment.

So few symptoms, on the other hand, may be produced by carcinoma of the stomach that the lesion usually passes the stage of operability or even of resectability before there is any definite localizing evidence of its presence. Neoplasms in the fundus or along the greater curvature may grow to large size before the patient is impelled to seek medical advice; neoplasms in the region of the pylorus, however, produce obstructive symptoms promptly and therefore are detected earlier in their course. In either case, interference with digestion and absorption of food and fluids will result and, together with the debilitating effect of the malignant lesion upon general health, will reduce the acceptability of the patient as a surgical risk.

The results of operative treatment for carcinoma of the stomach have improved considerably during the past few years, a greater number of patients being explored surgically and a higher percentage of resections being performed, either for palliation or with hope of cure. Maimon and Palmer,<sup>1</sup> for example, report that in a series of nearly 500 patients with gastric cancer, exploratory laparotomy was carried out in over 80 per cent and resection was performed in more than 40 per cent, of whom more than 70 per cent survived operation (chiefly subtotal gastric resection). Similar findings were reported from the Mayo Clinic.<sup>2</sup>

60 per cent of a somewhat larger series of patients with gastric carcinoma undergoing laparotomy, with a resection rate of 35 per cent and an operative mortality of less than 5 per cent in simple resections and less than 30 per cent in radical resections. Experience in general appears to indicate that a three-year survival rate can be expected in approximately one-fourth of the patients who recover from extensive gastric resections for carcinoma performed with the hope of cure. While this number is small indeed, it has nevertheless increased greatly in recent years; further improvement can be anticipated to follow increasingly early diagnosis of carcinoma of the stomach while the lesion is still localized and is producing relatively few symptoms.

Similar improvement has occurred in the surgical management of intractable or complicated gastric and duodenal ulcer. Subtotal resection of the stomach for gastric ulcer or resection of part of the stomach and the ulcer-bearing portion of the duodenum for duodenal ulcer formerly carried an average mortality rate as high as 15 to 20 per cent; in recent years, this figure has declined steadily to an average of less than 4 per cent and, in some clinics, of less than 3 per cent. While the improvement in operative results is due partly to technical improvements in performance of the operation, it is probably due chiefly to better understanding of the disturbed physiology in these patients and to better methods of care before and after operation.

Patients who enter the hospital for surgical correction of an intractable peptic ulcer or for removal of a carcinoma of the stomach usually give a history of digestive disturbance and interference with food intake over a period of many weeks. Even those who have been treated medically will exhibit some degree of chronic malnutrition, since ulcer diets in general do not provide an adequate and balanced intake of all the necessary nutritional factors. Many of these patients are in the older age groups and have other conditions such as cardiac disease, hypertension, arteriosclerosis, impaired renal function, or chronic bronchitis which will increase the risk of operation. Others are anemic following frequent losses of small amounts of blood from an active ulcer or a growing carcinoma, even though no single hemorrhage of noticeably large proportions has occurred. In practically all cases, weight loss, dehydration, malnutrition, hypoproteinemia, and avitaminosis can be expected; the patient with ulcer



has restricted his diet in an effort to reduce the gastric secretion and hence the ulcer pain, and the patient with carcinoma has reduced his food intake as a result of indigestion and loss of appetite consequent to the decreased secretion of gastric juice. The most serious dislocations of fluid and electrolyte balance are seen in patients with pyloric obstruction, the degree of physiologic disturbance depending upon the duration and the completeness of the obstruction.

### Preoperative Study

Patients who present one of the surgical complications of gastric or duodenal ulcer requiring emergency operation (p 627) receive only a minimum of preoperative investigation; those whose need for operation is less acute are prepared for surgery over a period of at least several days.

After the history has been taken and the physical examination completed and recorded, urinalysis is done and routine studies of the blood are made, including determination of the hematocrit values, hemoglobin estimation, red blood cell count, and white blood cell total and differential counts. Determinations are made of the plasma protein concentration and of the blood nonprotein nitrogen and chlorides. If there is any evidence of disturbed kidney function, a phenolsulfonphthalein excretion test and a Fishberg urinary concentration test are performed. Depression of liver function and liver glycogen are almost to be expected in these patients, whose diet has been restricted for so long; the hepatic function should be investigated in all chronically ill patients who are to undergo an operation as serious as gastric resection. The most generally useful liver function tests include the Quick hippuric acid excretion test, the cephalin-cholesterol flocculation test, and the fractional bromsulfalein test, elevation of the serum phosphatase may occasionally indicate extensive hepatic metastases in a patient with carcinoma of the stomach.

**GASTROINTESTINAL SERIES.**—Gastrointestinal series is done to secure as much information as possible concerning the location, type, and extent of the lesion, its effect upon the motility of the stomach, and the degree of pyloric obstruction. The gastrointestinal series is the most accurate method available for the diagnosis of ulcerative or space-occupying lesions of the stomach and

duodenum; with the help of expert fluoroscopic examination and spot films, a correct diagnosis can be made in more than 90 per cent of cases. As a rule, a barium enema is unnecessary unless the patient has definite complaints referable to the colon.

**GASTRIC ANALYSIS.**—Less use is made of gastric analysis as a diagnostic method since the greater dependability of roentgenologic studies has been established. Studies of gastric secretion may, however, afford information as to the state of activity of the gastric mucosa as well as some degree of confirmation of the x-ray diagnosis.

Normal gastric juice contains hydrochloric acid, pepsin, and mucin; its chief function is the digestion of protein foods, which are converted first to soluble acid metaproteins and then to proteoses and peptones by the action of pepsin in a sufficiently acid medium. The pH of the gastric juice normally varies from 1.0 to 1.5, free hydrochloric acid being present in amounts of 0.1 to 0.2 per cent (30 to 60 degrees or clinical units) and the total acid (free acid plus acid in loose combination with protein) amounting to 0.2 to 0.3 per cent or 60 to 90 clinical units. Pepsin is active only at pH values below 4.0; free hydrochloric acid therefore must be present in the gastric juice in appreciable quantities, since combined acid cannot lower the pH beyond 4.0. Medical control of hypersecretion in benign ulcer is based upon the administration of foods and medications to combine with the free hydrochloric acid and lessen peptic activity. On the other hand, the decrease in acid secretion and hence in peptic activity in association with carcinoma of the stomach is one of the reasons for the loss of appetite for meat, a characteristic early symptom of this disease.

Gastric juice is secreted rapidly following ingestion of food or following parenteral injection of histamine. Although both methods of inducing secretion for clinical analysis are in current use, the administration of histamine is more dependable, sometimes causing a flow of gastric juice when stimulation by food proves entirely ineffective. Gastric analysis is usually performed in the morning before breakfast when the patient has fasted at least eight hours. Determinations are made of the volume and of the free and total acid in the fasting specimen and in specimens removed thirty and sixty minutes following subcutaneous injection of histamine phosphate (0.5 mg.). In general, either hyper-

chlorhydria, with free hydrochloric acid in excess of 50 clinical units, or hypersecretion, with a total volume of gastric secretion above 100 c.c. in the fasting specimen, indicates the probability of benign ulcer. Low or absent acidity (achlorhydria) and diminished volume of gastric secretion suggest the probability that an ulcerating lesion of the stomach is malignant rather than benign. Gastric analysis is not a diagnostic test but is of confirmatory value only, carcinoma of the stomach may occur in the presence of normal or even of high gastric acidity, while benign ulcer may be associated with normal or low acidity and secretion. When no secretory response follows the injection of histamine, however, an ulcerative lesion of the stomach is almost certain to be malignant; benign ulcer rarely occurs in the presence of total anacidity.

### Preoperative Care

Patients with uncomplicated nonobstructing ulcers of the stomach or duodenum can be prepared for operation over as long a period as necessary to improve their surgical acceptability. After routine laboratory studies have been done, an attempt is made to restore as far as possible the patient's depleted physiologic reserves. Fluids are given in quantities of 2,500 to 3,500 c.c. each day until dehydration has been corrected; fluids are supplied by mouth in whatever quantity the patient is able to take, supplemented as necessary by infusions of dextrose (5 per cent) solution intravenously. If the patient has been vomiting or if depression of the blood chloride is present, isotonic salt solution is given intravenously in amounts not exceeding 1,500 to 2,000 c.c. daily until the deficiency has been corrected. When the plasma electrolytes have reached a stable normal level and the urinary output is maintained at 1,000 to 1,500 c.c. daily, determinations of the plasma protein level, the hematocrit level, and the blood cell counts are repeated.

Anemia is corrected by transfusion of blood until the hematocrit reaches 40, the red blood cell count is 4,250,000, and the hemoglobin is at least 11.6 Gm. (80 per cent). It is probable that simple clinical methods will soon be developed to determine total blood volume with reasonable accuracy so that the patient's hematocrit, hemoglobin, and total blood volume all can be re-

stored to actually normal rather than apparently normal levels before unusually severe operations are undertaken.

Because malnutrition is almost invariably present in these patients, administration of a high dietary intake of protein and carbohydrate is instituted, with additional vitamin concentrates. A liquid or semisolid bland diet is ordered, with frequent small feedings rather than three relatively large meals. An attempt is made to supply at least two to three times the normal daily intake of protein by administration every three hours of intermediate nourishments of skim milk powder or milk protein, with or without added carbohydrates and flavoring, in amounts of 30 to 45 Gm. (oz. 1 to 1½) in water. When the patient is unable or unwilling to take so much additional nourishment by mouth, protein hydrolysate solution can be given by vein in quantities of 50 to 100 Gm. daily. Vitamin preparations, especially vitamin B complex and vitamin C, are administered in full therapeutic dosage either orally or parenterally during the patient's entire hospital stay; vitamin K is given prophylactically for three days before and three days after operation.

**ACUTE INFLAMMATORY ULCER.**—Patients with acute inflammatory ulcer may be too ill to take sufficient food by mouth and may present a problem because of the severity of their pain. In such cases prompt relief can be obtained by administration of colloidal aluminum phosphate or aluminum hydroxide (1 per cent) by continuous drip. This preparation is given through a soft rubber nasal tube passed to the cardia and is administered throughout the day and night for seven to ten days at a constant rate of about 15 drops each minute. Considerable improvement usually is evident after the first full day of treatment and actual healing of the ulcer may occur by the end of the ten-day period. During the course of the continuous drip treatment, no food is given by mouth; alimentation is carried out entirely by the intravenous route. If the patient is unable to tolerate the tube after one or more days, the aluminum gel is given orally in doses of 4 to 8 Gm. in water each hour during the day and every two hours during the night. After the acute inflammation has subsided, a liquid or semisolid high protein-high carbohydrate diet is given, with feedings every one and a half to two hours until the patient is in satisfactory condition for operation.

Good results following the use of protein hydrolysate in treatment of patients with acute gastric or duodenal ulcer has been reported by Co Tui and associates.<sup>3</sup> According to this method, feedings are given every two hours either orally or by gastric tube, each feeding containing from 50 to 65 Gm. of completely hydrolyzed protein (for example, Protolysate) and approximately the same amount of a readily assimilable carbohydrate (for example, Dextrimaltose) in a glass of water. If eight such feedings are taken each day, the patient will receive from 300 to 400 Gm. of biologically complete protein daily, with sufficient carbohydrate to supply more than the required number of calories. The authors of the report state that of the small group of patients in whom the diet was tested, all had relief of pain within twenty-four hours, all gained a significant amount of weight within eight to ten days, and in all cases the acute ulcer was promptly brought to quiescence. Patients, however, are unwilling to take protein hydrolysate orally because of its unpleasant taste, which is difficult to disguise even with added carbohydrates and flavoring agents. Skim milk powder, which contains more than 35 per cent protein, or similar preparations with even higher milk protein content, may be used in equal or larger quantities also with good results.

Pain from acute inflammatory peptic ulcer is due partly to local inflammation and irritation and partly to reflex muscle spasm, both in the region of the ulcer and at the pylorus. The use of narcotic or sedative drugs for relief of pain is not advisable, and antispasmodic drugs such as atropine are not particularly effective. The greatest relief is afforded to these patients by frequent administration of compounds such as an aluminum gel, which neutralize the gastric acid and coat the surface of the ulcer, or of foods such as milk and cream or casein, which inactivate the gastric pepsin and afford dietary protein to encourage healing of the lesion.

As much time as necessary is taken to prepare the patient for operation; before surgery is undertaken fluid and electrolyte balance should be restored, the hematocrit should approximate a normal value, positive nitrogen balance should be attained by means of a high intake of protein and carbohydrate foods and of necessary vitamins, and local inflammatory reaction about the ulcer should be well controlled. If there has been no history of

recent pyloric obstruction, repeated preoperative gastric lavage is not necessary. In *all* cases, however, a Levin tube is inserted intranasally on the morning of operation and the gastric contents are aspirated. If an appreciable amount of old blood, mucus, or retained material is present, lavage is performed with warm normal salt solution or sodium bicarbonate (1 per cent). In every case the tube is allowed to remain until after the operation has begun to enable the anesthetist to remove by aspiration any air or saliva swallowed during induction of anesthesia. Most surgeons prefer to leave the tube in place during operation and for the following two to three days; some, however, prefer to remove it before the stomach is sectioned or opened.

An infusion of dextrose (5 per cent) solution is begun before the operation starts, so that a blood transfusion may be administered without loss of time if the need arises. Before a resection of the stomach is undertaken, at least 1,000 c.c. of blood should be available for immediate use during and after the operation.

**CARCINOMA OF THE STOMACH.**—Patients with carcinoma of the stomach present a somewhat different problem. Acute pain and inflammation are less likely to be present but digestion is more likely to be disturbed even though no obstruction has developed. Fatty foods, which are retained in the stomach for a relatively long time, are often somewhat distasteful to these patients and there is usually a loss of appetite for protein also because of the decrease in peptic activity. For this reason, the patient may be unable to take sufficient food, even in the form of skim milk or simple high protein nutritional supplements, to replace the tissue protein deficit or even to maintain a daily nitrogen balance. Under such circumstances the patient is encouraged to take as much as he can by mouth, and supplements of completely hydrolyzed protein with added carbohydrate are given in quantities of 30 to 45 Gm. (oz. 1 to 1½) every three hours for four to six doses each day. Feedings of protein hydrolysate in this quantity will supply from 125 to 250 Gm. of protein daily, without necessity for gastric digestion. If the patient is unable to take the preparation by mouth, it is worth while to administer it by Levin tube; if neither method proves satisfactory, one of the standard forms of protein hydrolysate for intravenous use is given by infusion in sufficient amounts to supply 100 Gm. of protein daily. Obviously, if obstruction or delayed emptying due to

carcinoma is present, no foods or liquids are given by mouth and all feeding is by the parenteral route.

Bacterial growth and protein decomposition may take place in the presence of gastric carcinoma because of the diminished secretion of gastric juice. Lavage of the stomach is therefore advisable at least once each day, with normal salt solution, sodium bicarbonate (1 per cent) solution, or hydrochloric acid (0.1 per cent). Nothing but water is given by mouth for the two days preceding operation and lavage is performed twice daily during this time and again just before operation to assure as clean an operative field as possible. As in the case of benign ulcer, the tube is allowed to remain in the stomach during induction of anesthesia and, according to preference, during and after operation.

**TOTAL GASTRECTOMY.**—The decision to remove the entire stomach is ordinarily made during operation, although in some cases the possible necessity for total gastrectomy can be foreseen. Presence of metastatic growth usually contraindicates such an extensive procedure. Preparation as previously outlined should be carried out over a period of seven or more days before operation, the vital capacity should be determined and an electrocardiogram secured, foci of infection (particularly around the teeth and gums) should be eliminated, and a high protein intake should be supplied even if it is necessary to do a preliminary jejunostomy<sup>4</sup> for feeding. Administration of either sulfadiazine or penicillin in full dosage is begun the day before operation and is continued into the postoperative period. A Levin tube is passed before operation either into the stomach or to the level of the lesion and lavage is performed. The tube is allowed to remain during operation until the esophagojejunal anastomosis is begun and is then withdrawn until the tip is 2 to 3 cm. above the proposed stoma. Suction is continued during and after operation. Transfusion of blood is necessary as a routine measure during the operation and immediately afterward.

**PYLORIC OBSTRUCTION.**—The presence of pyloric obstruction due to ulcer or carcinoma does not constitute an indication for emergency operation, even if the block is complete. As much time can be taken before operation as is necessary to improve the patient's condition. In most cases, moreover, the obstruction is due partly to nutritional or inflammatory edema, and proper treatment for two or three days will relieve the block enough to

allow passage of liquid food. A better response to treatment is obtained in obstruction due to acute inflammation and edema than in obstruction due to chronic scarring or to carcinoma.

The obstructed stomach is lavaged thoroughly at least once and preferably twice a day through a large (Ewald) tube. If lavage is performed only once daily, it should be done at night to enable the patient to rest comfortably. On each occasion the gastric contents are first aspirated and measured to determine the amount of residual and to detect any evidence of pyloric reopening. Large quantities of normal salt solution are used for lavage, the final irrigation being done with hydrochloric acid (0.1 per cent) if the patient has an acidity. As long as the pylorus is completely obstructed, nothing is given by mouth, the patient being allowed only to rinse the mouth with water.

Parenteral alimentation is carried out in the usual way, enough dextrose solution (5 per cent) and normal salt solution being given to insure a urinary output of 1,000 to 1,500 c.c. daily. Not over 1,000 to 1,500 c.c. of normal salt solution should be administered each day unless the blood chlorides are depressed, in order to avoid the possibility of salt retention and edema. To supply readily utilizable protein, one of the standard protein hydrolysate solutions (5 per cent) for intravenous use may be substituted for simple dextrose solution in sufficient quantity to supply from 50 to 100 Gm. of protein hydrolysate each day. Patients with peptic ulcer or carcinoma of the stomach severe enough to cause pyloric obstruction are almost certain to show anemia and depletion of total blood volume; transfusion of whole blood in relatively large amounts is usually necessary. Vitamin preparations, especially of B complex and C, are given in therapeutic doses, and vitamin K is given parenterally for three days before and three days after operation.

After several days the amount of residual material retained in the stomach will decrease and fluids will pass through the pylorus. At this stage small quantities of water with added lactose or Dextrimaltose and, if the patient will permit, with protein hydrolysate, can be given in sufficient amounts to replace one of the intravenous infusions, with consequent psychologic as well as physiologic improvement. Gastric lavage is continued as before until maximum improvement is obtained, the amount of liquid diet supplied being increased in proportion to the relief of ob-



struction. Preparation of this type is absolutely necessary before operation can be undertaken; the obstructed stomach is dilated and atonic and the gastric tissues are too edematous and soft to hold sutures safely. During the two days just before operation, constant gastric suction is maintained by means of a Wangensteen suction apparatus. Periodic lavage can be carried out through the Levin tube at this time; it is especially important to lavage the stomach just before operation, using hydrochloric acid (0.1 per cent) for the final rinsing.

### Postoperative Care

Routine postoperative orders following gastric resection or gastroenterostomy include morphine, 10 to 16 mg. (gr.  $1/6$  to  $1/4$ ), hypodermically as needed for pain, not oftener than every four hours during the first thirty-six hours. Individual or "stat" orders for narcotics or analgesics are left after this time. The patient is placed flat in bed and his position is changed from side to side each hour when awake; Fowler's position may be assumed if desired for comfort. To decrease the likelihood of pulmonary atelectasis, carbon dioxide (5 to 10 per cent) inhalations, administered until the patient takes several deep breaths in response to the stimulus, may be given every one to two hours for twenty-four hours after operation. If carbon dioxide is not available, the patient is requested to take at least ten full deep breaths each hour, under direct supervision of an attendant. Oxygen, either by tent or by nasal catheter, is of supportive value in older patients, in patients with cardiac or pulmonary damage, or in patients who have been operated upon by a thoracic approach.

The Levin tube inserted preoperatively is usually allowed to remain in the stomach during and after operation; it is connected to a Wangensteen suction apparatus as soon as the patient is returned to his room. Most surgeons prefer to leave the tube in place for thirty-six to forty-eight hours, until the danger of postoperative gastric retention or of acute gastric dilatation is past. Gastric suction also gives immediate indication of postoperative intragastric bleeding, when present, and minimizes leakage from any small defect or opening that may be left in the gastrointestinal anastomosis until spontaneous healing has an opportunity to take place. Other surgeons consider constant drainage to be

unnecessary and uncomfortable and prefer to pass a tube and aspirate the contents of the stomach at intervals of twenty-four hours until gastric peristalsis is re-established, unless specific indications for constant suction should arise.

From 500 to 1,000 c.c. of blood are lost during the average gastric operation; a transfusion is given routinely during the first few hours following operation as well as during operation. Enough blood is administered during the postoperative course to restore the hematocrit to normal; although transfusion of this much blood may be expensive, it reduces the possibility of post-operative shock, speeds the healing of the area of operation and the return of gastric function, and shortens the hospital stay and the duration of convalescence. Hematocrit determinations or, if possible, complete blood counts are made at intervals of three to four days until the blood constituents have reached a stable normal level.

Early ambulation will speed the rate of convalescence. If recovery has progressed smoothly, the patient can take several steps with assistance two days after operation; the amount of exercise is increased regularly on succeeding days. Patients who recover less promptly or who are too apprehensive to attempt early ambulation are kept in bed for ten to twelve days before arising.

**Diet.**—Most surgeons devise their own routine progressive gastroenterostomy diets, of which the following is probably typical:

Nothing is given by mouth for twenty-four hours after operation. On the following day the patient is allowed to take sips of water every hour, not over 30 c.c. being given each time, although the amount may be increased to 60 c.c. by evening. After two days the stomach tube is clamped off for several hours, following which the gastric contents are aspirated. If no gastric retention is present, the tube is removed; if fluids taken orally while the tube was clamped have accumulated in the stomach, suction is continued and food is withheld until peristalsis returns.

A surgical liquid diet is begun on the third day, the patient being permitted to have broth, bouillon, weak tea, and water on alternate hours in amounts of 60 cubic centimeters. The Levin tube is passed on the third night and the contents of the stomach are aspirated to determine if emptying is satisfactory. If an ap-

preciable residual is present, the diet is discontinued and suction is again instituted for as long as necessary.

Malted milk and milk without cream are added to the diet on the fourth and fifth days, and the quantity permitted is increased to 100 cubic centimeters. Water is allowed as desired. On the sixth and seventh days, soft-cooked cereals, custards, ice cream, Jello, and soft-cooked eggs are added, in very small amounts at first and increasing in quantity gradually at each feeding according to the patient's appetite. Small portions of toast and baked potato are given on the eighth day, the patient at this time being on a full semisolid diet in restricted quantities. No more additions are made to the diet until the thirteenth or fourteenth day, when a surgical soft diet or low-residue solid diet is ordered, the quantity of each feeding to be regulated by the patient's appetite. This diet is continued until convalescence is complete.

Until fluids can be taken orally in sufficient quantities, infusions must be given to assure a total intake of 2,500 to 3,500 c.c. daily or enough to maintain the urinary output at the optimum level of 1,500 cubic centimeters. Protein hydrolysate solution (5 per cent) for intravenous use, with or without added dextrose, is of value in this type of patient; dextrose solution (5 per cent) is used to supply the major portion of the fluid intake. If normal salt solution is administered, 1 liter each day will supply adequate sodium chloride; larger amounts may cause salt retention and edema. Parenteral preparations of vitamins B complex and C are continued in therapeutic dosage until the patient is able to take them orally; vitamin K is necessary for only three days after operation.

Co Tui and co-workers<sup>3</sup> have advocated a plan of hyperalimentation following gastric resection with which they report excellent results. Since ulcer patients, especially in the postoperative period, show a well-marked chronic protein deficiency as well as a negative nitrogen balance, an attempt is made to feed approximately four times the amount of protein normally required (1 Gm. per kilogram of body weight per day) to maintain nitrogen balance. Completely hydrolyzed protein (for example, Protolysate), which requires no gastric digestion and is readily soluble in water, therefore is supplied in quantities approximating 5 Gm. per kilogram of body weight per day throughout the postopera-

tive period, with added carbohydrate (Dextrimaltose) in sufficient amounts to provide an adequate caloric intake. An infusion of protein hydrolysate (Amigen, 5 per cent) in dextrose solution (5 per cent) is given during the first twelve hours after operation, following which feedings are introduced through the gastric tube, 30 c.c. being given each hour for six hours and then 50 c.c. each hour for a similar period. Amounts of 60 to 90 c.c. are given hourly on the second postoperative day and from 90 to 100 c.c. each hour thereafter for two weeks. Intravenous fluids are needed for the first three days only; enough is supplied orally after this time to make up the required caloric and fluid intake. Therapeutic doses of vitamins B complex and C are administered daily. In comparison with a control series of similar patients fed with the usual postgastrectomy diet, the patients on the hyperalimentation regimen showed a positive nitrogen balance, a steady gain in weight, and a prompt recovery of strength.

It should be noted that in this study feedings were administered during the first few days by means of an Abbott-Rawson<sup>4</sup> double-lumen tube. This tube (Fig. 63) consists of a 12 French tube within a 16 French tube, each opening separately at each end. The smaller tube projects far enough beyond the termination of the larger tube to permit its insertion at operation through the gastroenterostomy stoma and for a distance of twelve inches into the distal jejunal loop; it is used for introduction of nutrient fluids directly into the jejunum during the first days of the postoperative period. The outer or encircling tube is perforated near its termination, the perforated portion remaining in the stomach for simultaneous suction drainage. It functions therefore as a nonoperative jejunostomy for feeding purposes.

The studies of Co Tui and associates have provided a real contribution in demonstrating the effectiveness of early postoperative feeding of readily assimilable protein and carbohydrate in large quantities, a therapeutic measure which is not possible with the more generally employed surgical liquid and semisolid diets. Even when the standard postoperative progressive diet is employed, it can be amplified to good effect by the administration of infusions of protein hydrolysate solution and the introduction of small amounts of protein hydrolysate-carbohydrate solutions through the stomach tube at frequent intervals during the early postoperative period. After the tube has been removed the pa-

tient may be reluctant to take supplementary protein hydrolysate feedings because of the disagreeable taste. Much the same effect can be attained by substitution of milk protein or skim milk powder in water in somewhat larger dosage throughout the remainder of convalescence.

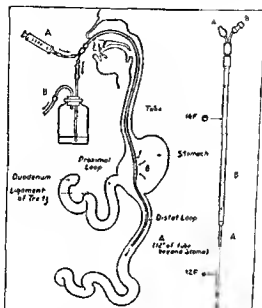


Fig. 63.—A line drawing showing use of the Abbott-Rawson tube in gastrectomy cases (From Co Tui and others. *Ann Surg* 120:90, 1914, J B Lippincott Co.)

In a preliminary report by Hollander and associates<sup>7</sup> a similar diet of predigested aliment has been suggested for feeding by jejunostomy. These authors advocate the establishment of a preliminary jejunostomy in patients who are not satisfactory risks for gastric resection because of prolonged starvation and dehydration or because of acute inflammatory changes in the region of the ulcer. Similarly, the suggestion is made that a complementary jejunostomy, performed in poor-risk patients at the time of gastric resection, can be used to good advantage for feeding in the early postoperative period. The mixture devised for jejunostomy feeding contains in each liter completely

hydrolyzed protein (for example, Protolysate), 85 Gm., a carbohydrate preparation composed of dextrans and maltose (for example, Dexin), 150 Gm., inorganic salts, B complex and C vitamin preparations, and cream, 85 c.c. (added, with shaking, just before use). The diet is administered through the jejunostomy by means of a drip gravity apparatus at a rate varying from 30 to 125 c.c. each hour, according to the patient's tolerance; it is diluted with normal salt solution and given more slowly during the early postoperative period. Although no closely controlled studies were made, the authors report that clinical response following use of the mixture was excellent in the small group of cases presented.

It would appear worth while, however, to try nonoperative methods of alimentation (gastric drip, tube feeding, supplementary infusions) before a jejunostomy is made for this purpose. When a jejunostomy is necessary, as in the case of unrelieved pyloric obstruction in a patient who is not in acceptable condition for gastric surgery, a well-planned alimentary mixture such as that described will be of the greatest value.

**Total Gastrectomy.**—The mortality of total gastrectomy is generally far higher than that of subtotal removal of the stomach; the operation is performed through either a trans-thoracic or a transabdominal approach. Postoperative shock, cardiac failure, pulmonary atelectasis, pneumonia, pulmonary embolism, leakage from the anastomosis, peritonitis, and feeding difficulties are all more likely to occur in this type of patient; close watching is necessary, particularly during the first week after operation.

Oxygen in high concentration is administered throughout the operation and is continued without interruption during recovery from anesthesia and the early postoperative period. An intranasal catheter is used until consciousness returns, after which a mask may be substituted if higher concentrations of oxygen are desired. Especially close watch is kept for the earliest evidence of pulmonary atelectasis, the chest being examined by auscultation twice a day for several days after operation.

The patient is placed either on his back or his left side (operated side), with the bed in the Trendelenburg position. At least twelve inches of elevation of the foot of the bed is advisable, both to promote drainage from the esophagus and to relieve

tension on the esophagojejunal anastomosis. This elevation is maintained for three days following operation, unless there is too much interference with respiration. Following transthoracic gastrectomy the intercostal drainage catheter is fixed with a rubber sponge dressing (p. 555) and is attached to a constant suction apparatus with gentle suction (7 to 10 cm. of water) for three or four days until drainage is minimal. The catheter is then withdrawn and a small dressing is fixed snugly over the remaining wound to prevent entry of air during respiration. A portable x-ray plate of the chest is taken a day or two after removal of the catheter. Subsequent collections of fluid are removed by thoracentesis; as in all intrathoracic operations, the postoperative development of a pleural effusion or even of empyema is a possibility. Penicillin in full therapeutic dosage, begun the day before operation, is continued without interruption for five days after operation as a prophylaxis against infection.

The Levin tube, passed before operation and allowed to remain with its tip several centimeters above the anastomosis, is connected to a Wangenstein suction apparatus and left in place for from five to seven days. During this time nothing is given by mouth; feeding is done entirely by vein, with protein hydrolysate solution and dextrose (5 per cent) solution supplemented by blood transfusion until the hematocrit is within a normal range.

Oral feeding is started a week after operation, beginning with water, 15 c. c. (oz.  $\frac{1}{2}$ ) every hour and increasing gradually and progressively in amount. Surgical liquid diet is begun on the ninth day, including protein hydrolysate solution if the patient will accept it. By the fourteenth postoperative day, small amounts of custard, Jello, ice cream, and cereal can be added to the diet, and the quantity of fluid permitted can be increased to 60 c. c. (oz. 2) each hour. Skim milk or milk protein supplements are of particular value during this period. After three weeks a semisolid diet can be ordered, with very small servings specified. During the entire period of convalescence to normal health, efforts are made to keep the protein intake at as high a level as possible, protein hydrolysate solution being given by vein daily during the first three weeks and supplementary high protein feedings for several weeks thereafter. The patient is

most comfortable in the erect position following meals; some regurgitation may occur if he lies down.

Therapeutic doses of vitamins B complex and C are instituted before operation and continued throughout convalescence; maintenance doses are administered indefinitely. Vitamin K is given for three days before and three days after operation. Because occasional reports have appeared of chronic iron-deficiency (secondary) anemia and even of macrocytic hyperchromic (pernicious) anemia following total gastrectomy, ferrous sulfate in liquid form (elixir) and liver concentrate or extract are given routinely for an indefinite period, beginning three weeks after operation.

Of those patients who survive operation,<sup>8</sup> approximately 50 per cent will live a year or more; from 10 to 20 per cent will probably survive for at least three years.

**Postoperative Complications.**—Although formerly high, the incidence of serious complications after gastric surgery has been markedly reduced following improvement in preoperative and postoperative care.

**POSTOPERATIVE SHOCK.**—Postoperative shock occurs most often in debilitated, undernourished, or anemic patients; it is most likely to develop if preoperative preparation has been inadequate or if the operation has been long and difficult. Deep and prolonged anesthesia, insufficient oxygen during anesthesia, loss of blood without proper replacement, and partial obstruction of the respiratory tract are factors which predispose to postoperative shock. Premonitory signs include slow recovery or prolonged depression following anesthesia, subnormal temperature and blood pressure, elevated pulse rate, and definite apathy, weakness, and pallor. Treatment of shock, never as satisfactory as prevention, is most effective in the early stages and consists of measures usually employed to combat secondary or surgical shock from any cause.

Hemorrhage from the operative field is uncommon; the fluid aspirated from the stomach through the inlying Levin tube is always blood stained for a day or two after operation, but appreciable amounts of bright red blood are not often noted. Bleeding from the field of operation is rarely severe and rarely persists for more than a few hours. Leakage of blood usually stops promptly following administration of a transfusion of



fresh whole blood, if vitamin K has not been given preoperatively, it may be well to draw a sample of blood for prothrombin time determination and to administer a therapeutic dose of vitamin K parenterally at once. Gastric suction is continued and the stomach is kept empty. If the bleeding is dangerously profuse, transfusions are given and the patient is returned to the operating room. The wound is reopened, an incision is made in the wall of the stomach, and a continuous suture is placed around the stoma for hemostasis; the gastrotomy is then closed. Rarely, hemorrhage may occur from a gastric or duodenal ulcer that was not removed at operation. Such a complication occurring in the immediate postoperative period cannot be foreseen; if the hemorrhage is of significant degree, the prognosis is not good. Management of the patient is carried out according to the usual plan for treating ulcer hemorrhage (p. 627).

**PULMONARY ATELECTASIS.**—In chronologic order pulmonary atelectasis is the next complication that may be anticipated in the postoperative period, occurring within the first three to four days following operation. Particularly common after upper abdominal procedures, massive collapse of a lung is marked by respiratory difficulty, fever, tachycardia, and evidences of anoxemia. The physical signs are characteristic (p. 360), and the condition usually is recognized without difficulty; it responds well to proper treatment, which should be instituted without delay to prevent progression of atelectasis into bronchopneumonia.

**ACUTE GASTRIC DILATATION.**—Acute gastric dilatation will not develop as long as the stomach is kept empty by suction drainage. This complication is most likely to occur when gastric suction is not used after operation, dependence being placed upon insertion of a Levin tube once or twice a day to empty any residual accumulation that may be present. As a rule, intermittent gastric aspiration is sufficient; occasionally, however, acute dilatation will appear and may develop gradually over a period of several hours or, less commonly, suddenly within a few minutes. Dilatation of the stomach occurs within the first three days after operation; rarely, it will develop after removal of the nasal tube from a patient who has been treated by routine gastric suction drainage. The complication is not serious if it is recognized promptly and treated immediately, but it is dangerous

if allowed to progress. Acute gastric dilatation occasionally occurs in association with generalized peritonitis.

The patient with an acutely dilated stomach (p. 451) typically vomits a large quantity of brownish-black watery fluid, although profound prostration may develop before vomiting occurs. Examination reveals a rapid, running pulse, subnormal temperature, and depressed blood pressure, the picture somewhat resembling incipient shock. The copious vomiting is sufficient indication for passage of a Levin tube without delay; proper treatment consists of aspiration of the gastric contents, institution of gastric suction drainage, and replacement of the lost fluids and electrolytes. Feeding, if already begun, is stopped and the stomach is kept decompressed until peristalsis returns.

**OBSTRUCTION OF THE GASTROENTERIC STOMA**—Obstruction of the gastroenteric stoma is no longer common. Formerly thought to be caused by errors in operative technique, stomal block is now believed to be due more frequently to nutritional edema. Depletion of tissue and plasma proteins and of vitamin B, so often seen in patients whose diet has been sharply restricted by gastrointestinal tract disease, is likely to cause swelling and edema around the suture line, sometimes sufficiently pronounced to produce partial or complete obstruction of the stoma. Gastric retention on this basis ordinarily appears within the first post-operative week, although the stoma may function normally for the first few days and develop a block during the second week. In an occasional case the obstruction is actually due to a mechanical cause; during performance of gastrojejunal anastomosis, the stomach is drawn strongly downward and if the jejunal loop is made too short, kinking may occur when tension on the stomach is released. It is preferable, however, to administer the lacking nutritional factors in proper quantities for several days before a final diagnosis is made. Therapy consists simply of transfusion of blood until the hematocrit reaches a normal level, infusion of protein hydrolysate solution in amounts sufficient to supply 100 Gm. or more of protein each day, and administration parenterally of therapeutic doses of vitamins B complex and C. If the obstruction is due to mechanical causes, prompt operative correction is necessary.

**LEAKAGE FROM THE DUODENAL STUMP**.—Leakage from the duodenal stump is one of the most frequent causes of death

following gastric resection and is the complication most feared by the surgeon. In most cases of duodenal ulcer, operation for resection is done only after medical treatment has failed and the ulcer is producing obstruction, or intractable pain due to acute inflammation or perforation into the pancreas, or is the site of serious hemorrhage. Because of the extent of such a lesion and the scarring and inflammation of the surrounding tissues, closure of the duodenum following resection of the ulcer is technically difficult and leakage may occur. Various methods of closure have been advocated, all designed to achieve security by mobilization of sufficient duodenum to permit inversion by two rows of sutures, the inner row usually being of chromic catgut and the outer of silk or cotton.

Different explanations for duodenal stump leakage have been proposed, such as the necrotizing effect of pancreatic secretion exuding from the traumatized areas in the pancreatic capsule, insecure closure because of insufficient duodenal stump available for proper suturing without tension following removal of the ulcer, and back pressure of accumulating duodenal secretions in the duodenojejunal loop proximal to the stoma. In order to secure sufficient duodenum for closure in two layers, most surgeons mobilize 2 to 4 cm. of duodenum away from the underlying pancreas. Shapiro and Robillard<sup>9</sup> believe this practice to be unsafe since the mural arteries supplying this portion of the duodenum are vasa recta with few anastomotic branches; mobilization of the duodenum by dissection from the pancreas therefore will interrupt several terminal arteries and the freed segment may be devitalized. These authors state that unless serosal inversion is performed beyond the point at which the duodenum still remains attached to the pancreas, the inverted portion is liable to become necrotic, with consequent leakage. A similar comment is made by Rienhoff.<sup>10</sup>

Duodenal leakage appears from four to ten days after operation. Leakage into the peritoneal cavity is likely to be fatal; however, leakage may be sufficiently slow to permit some degree of walling-off of the leaking area, with drainage through the abdominal incision and establishment of an external duodenal fistula. An increasingly profuse drainage of pungent, foul, watery, bile-stained fluid exudes from the incision, and digestion of all the layers of the wound and the surrounding skin area

promptly ensues. If the fistula is very small, the drainage is scant in amount and ceases after a few days. More often, however, the defect in the duodenal stump is larger and more serious; the complication generally is difficult to manage and carries a high mortality rate.

The duodenal fluid contains pancreatic digestive enzymes and bile in addition to other secretions. As soon as the condition is diagnosed, immediate steps should be taken to prevent damage to the abdominal wall. Dressings are removed, a cradle and heat tent are employed, and the abdomen is allowed to remain exposed to encourage prompt drying. Aluminum paste or powder is applied to the skin over a base of compound tincture of benzoin or rubber cement and suction drainage is instituted. Drainage is accomplished best by means of powerful suction applied to a small tube within a perforated metal sheath (sump drain) passed as far as possible through the gap in the wound to the leaking area. Insertion of a simple tube or catheter is likely to be unsatisfactory; the tissues of the wound margins are sucked into the catheter openings immediately and render it ineffective. If a single tube is used, a small puncture hole should be made above the skin level, both to minimize suction on the wound margins and to prevent excessively strong suction. Suction by gravity siphonage, as from a Wangensteen suction apparatus, is entirely insufficient; powerful aspiration must be applied constantly either by means of an electric motor or water pump suction apparatus. Some protection may be afforded by passing the suction tube through a small hole in a piece of rubber dam, fastened to the skin up to the edges of the fistula by means of rubber cement or dermatome adhesive; this cannot be done after excoriation has developed. Small amounts of duodenal juice will leak onto the abdomen even when suction is efficiently applied; application of powdered casein, protein hydrolysate, or skim milk will inactivate the secretions more effectively than compresses of dilute hydrochloric acid. Close watch and constant care is most needed during the first day or two after appearance of the fistula, since it is easier to prevent damage to the skin by digestion than to treat it after it has developed.

If food or fluids are given orally in the presence of a large duodenal fistula, an increased amount of digestive fluid mixed with food and mucus pours from the opening. Constant gastric

suction therefore is instituted and nothing is given by mouth. Since an extensive duodenal defect may persist for several weeks, a high jejunostomy is necessary for feeding and should be performed promptly. A suitable nutritional mixture can be made by combining protein hydrolysate, Dextrimaltose or Dexin, and therapeutic doses of vitamins A, B complex, and C in sufficient quantity in dilute solution to supply from 2 to 4 Gm. of protein per kilogram of body weight per day with enough carbohydrate to make up a total of 2,000 to 3,000 calories daily. As the patient's condition improves, cream (to supply fat) can be mixed with the feeding just before administration (p. 614). Jejunostomy feedings are given by continuous drip through an apparatus similar to that used for administration of aluminum phosphate gel to patients with acute peptic ulcer; the rate of flow varies from 50 to 100 c.c. per hour, depending on the patient's general condition and intestinal function. Hydrolyzed protein is preferable because no tryptic digestion is necessary; a higher carbohydrate is more satisfactory than simple dextrose, which requires no digestion but is likely to cause distention and diarrhea.

Large quantities of body fluid and electrolytes may be lost each day through a duodenal fistula. An accurate fluid intake and output chart is an absolute necessity in the care of such a patient, and frequent determinations should be made of the blood chloride, blood nonprotein nitrogen, and plasma protein concentrations as well as of the blood carbon-dioxide combining power. Hematocrit determinations and red and white blood cell counts are indicated to detect evidence of hemoconcentration, anemia, and infection. Daily urine studies should include determination of total volume output and specific gravity and qualitative albumin tests. Penicillin is given parenterally in full therapeutic dosage from the time the fistula first develops and is continued until all evidence of local inflammation has subsided.

Until jejunostomy can be performed, fluid and metabolic needs are met by *intravenous feeding*. From 50 to 100 Gm. of protein hydrolysate and 150 to 250 Gm. of dextrose can be supplied by vein and will suffice until the jejunostomy is functioning adequately, after which daily intravenous supplements can be administered to keep the protein intake as high as possible. Sodium chloride is lost with the duodenal fluid and must be

replaced in proper amounts. Different commercial preparations of protein hydrolysate have different salt contents; the amount present in the compound being used should be noted in the computation of daily salt intake. Blood and plasma given as transfusions also serve as a source of salt intake, supplying 5 to 6 Gm. per liter. Since the sodium chloride content of digestive fluid is approximately half that of normal salt solution, not over 1,000 to 3,000 c.c. of normal salt solution each day will be needed to replace the salt loss and may be administered by jejunostomy as well as parenterally. Frequent determinations of the blood chloride concentration and, in case of doubt, of the urinary chloride excretion should be made to assure adequate salt replacement and to prevent excessive intake with consequent salt retention and edema. Enough fluid is given to promote excretion of from 1,000 to 1,500 c.c. of urine each day.

Because of the debilitating nature of duodenal fistula complicating an extensive gastric resection, anemia is likely to develop. Even though sufficient blood has been given during and immediately after operation, further transfusion will be necessary later in the course of convalescence.

Body fluid and nutritional balance are maintained better if the secretions lost through a duodenal fistula are restored to the intestinal tract. The juices draining from the duodenum may amount to from 1,000 to 5,000 c.c. each day; as this fluid is collected by the suction system, it is restored through the jejunostomy. Although collection and return of the secretions is unnecessary if the fistula is small and drainage is slight, it is of definite value in the care of patients with large fistulas.

Attempts at operative closure of the duodenal opening are not advisable; necrosis, edema, and inflammatory reaction about the fistula are too extensive to permit surgical repair. After several months have passed and scarring has occurred, any remaining traces of the fistula may be studied and operation considered at that time but not before all signs of tissue reaction have disappeared and maximum spontaneous healing has occurred.

**OTHER COMPLICATIONS.**—Other complications which may occur after any laparotomy tend to be somewhat more frequent after gastric surgery because of the generally substandard condition of the patient, the seriousness of the procedure, and the

times and requiring a short period of rest immediately after meals.

Particular stress should be placed upon ingestion of a high protein diet, supplemented by frequent small feedings of powdered milk protein, protein hydrolysate, or skim milk powder in water. Antispasmodics such as atropine are of little value but may be tried. It is of interest to note that occurrence of a typical "dumping syndrome" following transthoracic resection of the vagus nerves was reported by Moore and associates,<sup>11</sup> the operation having been performed for jejunal ulcer following gastroenterostomy. It appears, therefore, that the vagus nerve is not an essential part of the nervous pathway involved in this syndrome.

**ANEMIA.**—Anemia subsequent to gastric resection is ordinarily of the hypochromic microcytic iron-deficiency type and probably is due to interference with absorption of dietary iron. Macrocytic (pernicious) anemia does not commonly follow even total gastric resection, perhaps because the intrinsic antianemic factor is produced also in the jejunum. Ferrous iron in solution is given routinely following extensive gastric resection; crude liver extract also is supplied on an empiric basis. Therapeutic doses of the necessary vitamins, particularly A, B complex, and C, are prescribed for an indefinite period. While measures such as these, together with an adequate high protein diet, should be sufficient to maintain normal red cell and hemoglobin values, some patients will develop anemia of moderate to severe degree that will respond to nothing less than an occasional blood transfusion.

**MARGINAL (ANASTOMOTIC) ULCER.**—Marginal (anastomotic) ulcer following gastric resection or gastroenterostomy develops within a matter of months following operation and is a purely surgical problem rather than a consideration of postoperative care. Patients with this complication usually exhibit a high gastric acidity with increased night secretion and show a marked loss of weight and strength as a result of interference with intake and digestion of food. A relatively long period of preparation is required before operative repair is undertaken. Particular attention is paid to restoration of normal blood volume and hemoglobin content, and large amounts of protein (3 to 5

Gm. per kilogram of body weight per day) are administered by oral feeding or by intragastric drip to reduce the inflammatory reaction around the ulcer and to encourage a healing response before operation is attempted. Full doses of vitamins B complex and C also are of value in these patients.

### Ulcer Complications

**Ulcer Hemorrhage.**—Choice of medical or surgical treatment for acute hemorrhage from peptic ulcer may be one of the most difficult problems to confront the physician. No consistently dependable criteria have yet been established to determine in each case whether the bleeding will be fatal if not promptly checked or whether it will respond to nonoperative treatment. Heuer<sup>14</sup> reports that of 337 patients hospitalized for ulcer hemorrhage, twenty-seven (8 per cent) died; of these, eighteen were too acutely ill even to warrant surgery. The other nine deaths represented 29 per cent of thirty-one patients operated upon during acute massive hemorrhage, from which it is assumed that all would have died without emergency surgery. The conclusion is reached that hemorrhage from peptic ulcer will be fatal or potentially fatal in approximately 15 per cent of cases, a figure which is in general accord with most other published statistics. It is safe to say, therefore, that not more than one in six patients admitted to the hospital for ulcer hemorrhage will require emergency surgery upon admission.

The site of the ulcer, the duration and rapidity of blood loss, the past history, and the age, sex, and general condition of the patient all are considered in reaching a decision as to therapy. Patients rarely die from the first hemorrhage, particularly if they are in the younger age groups (under 50 years) and if the ulcer is not of the chronic, medically intractable type. On the other hand, patients over 50 years of age are more likely to show arteriosclerotic changes in the vessels which will hinder retraction of the medial coats of the eroded artery and interfere with clotting. Older patients are likely also to have some degree of cardiorenal damage which will be intensified by the falling blood pressure and impaired oxygen supply secondary to massive hemorrhage.

Chronic ulcers intractable to medical treatment are characterized by dense scarring and deep erosion into the surrounding tissues; massive hemorrhage from an ulcer of this type usually



requires immediate operation, especially if a history of repeated bleeding is present. If located on the posterior duodenal wall, such an ulcer may erode into the underlying gastroduodenal artery; if on the lesser curvature of the stomach, erosion of a branch of the left or right gastric artery may take place. Similar ulcers in other locations are less likely to involve large arterial branches, while acute ulcers in any location are more likely to produce bleeding from small vessels in the mucosal or muscular layers than from the more externally situated large vessels. While bleeding caused by acute ulcers occasionally may prove fatal, there is usually a good response to conservative management.

Patients admitted to the hospital for ulcer hemorrhage are put at complete bed rest and no visitors are permitted. Morphine sulfate is administered either intravenously in a dose of 8 to 10 mg. (gr.  $1/8$  to  $1/6$ ) or hypodermically in a dose of 10 to 16 mg. (gr.  $1/6$  to  $1/4$ ), repeated as necessary. If the patient is nauseated by morphine, another narcotic such as Dilaudid or Demerol (p. 91) may be substituted or a barbiturate may be given hypodermically. Nothing is permitted by mouth, not even cracked ice or sips of water. Gastric lavage is inadvisable, although if the patient is retching because of retained blood in the stomach, a Levin tube may be passed and simple aspiration of air and fluid performed. Hematocrit determinations and complete blood counts are made on admission and are repeated at frequent intervals as indicated; the blood pressure and pulse rate are taken every two hours. A transfusion of fresh whole blood is started at once and is administered continuously at the rate of 40 to 50 drops a minute until a favorable response is noted or until operation is scheduled, when the rate of administration can be increased slightly. Although it was formerly believed that transfusion in ulcer hemorrhage might increase bleeding or dislodge a developing clot, the present practice is to replace the lost blood slowly enough to avoid a rapid rise in blood pressure but rapidly enough to keep the pressure above shock level and to maintain an adequate blood supply to the viscera. Fresh blood is preferable to bank blood because of its higher prothrombin content. It is advisable also to administer therapeutic doses of vitamin K (2 to 4 mg.) intramuscularly or intravenously in case hypoprothrombinemia should be present. Large quantities

of blood by transfusion are necessary in patients who have had massive hemorrhages.

Most patients will respond well to transfusion and gastric inactivity. In such cases, surgical liquid diet, fortified with gelatin, powdered milk protein, skim milk, or, if possible, with protein hydrolysate, is given in small quantities frequently, beginning about three days after hemorrhage has ceased. Progressive increase in diet is made according to the preferences of the physician; the usual gastroenterostomy diet routine or the Sippy diet without medication will be satisfactory in most cases.

Patients under 50 years of age, with an acute ulcer history or experiencing their first ulcer hemorrhage, will respond as a rule to conservative treatment. Patients older than 50 years, with a history of chronic ulcer and medical intractability or of repeated episodes of bleeding or with long-standing ulcer of the posterior duodenal wall or lesser curvature of the stomach are likely to require immediate operation if the hemorrhage is massive or if prompt response to conservative therapy does not occur. Surgical mortality is lowest if operation is performed within twenty-four or at most forty-eight hours after onset of bleeding. Further delay is unnecessary since continuing hemorrhage can be recognized within this time and since the response of bleeding patients to transfusion is poor after the circulating blood volume has been severely depressed for more than a few hours or the gastrointestinal tract has become filled with coagulated blood. Patients entering the hospital in incipient or fully established shock are admittedly poor operative risks, but if cessation of hemorrhage and elevation of blood pressure do not follow transfusion promptly, their chances of recovery are a great deal better if the bleeding is stopped surgically than if ineffective conservative treatment is continued until surgery is impossible. Some patients, usually in the older age groups, will respond temporarily to nonoperative management but will develop a second hemorrhage one to two weeks after the first. In these cases, surgery is required and should be performed as soon as possible.

The type of operation performed depends to some extent upon the condition found at operation. Transduodenal or transgastric suture of the bleeding point and ulcer surface is the simplest procedure but may be followed later by further hemorrhage.

Subtotal gastric resection with removal of the ulcer is the best procedure but is likely to place a severe strain upon the weakened patient, especially if the ulcer is acutely inflamed. Operation upon these patients carries a high mortality rate but is the only recourse when hemorrhage is massive or conservative methods fail.

No special measures of preoperative or postoperative care are necessary; the transfusion begun on admission is continued during and after operation until normal blood values are approached. Vitamin K (menadione) is supplied intramuscularly or intravenously in doses of 2 to 4 mg. daily and full doses of vitamins B complex and C are added to the infusions, which are given following operation in amounts sufficient to insure an adequate urinary output. Administration of penicillin is begun upon admission and is continued for several days. Nothing is given by mouth for twenty-four hours, after which a standard gastroenterostomy diet is instituted. An enema may be given on the fourth postoperative day to remove the irritating partially digested blood from the colon.

**Acute Perforation.**—The largest single cause of death from peptic ulcer is acute perforation, which is necessarily treated as a surgical emergency. Although the operative mortality in general averages at least 20 per cent, rates as low as 6.3 per cent<sup>15</sup> have been reported. Improvement in results of surgery are attributed to several factors, particularly prompt hospitalization of the patient, adequate preoperative preparation, minimal operative procedures, proper postoperative care, and systemic use of antibacterial agents.

Surgery is most successful if performed within four to six hours after acute perforation has occurred, but since the patient is usually admitted in a state approaching shock, certain preoperative measures are necessary. An infusion of dextrose (5 per cent) and normal salt solution is begun at once, while a blood transfusion is prepared for administration as soon as possible. If the diagnosis is definite and immediate operation is scheduled, the patient can be given morphine, 10 mg. (gr. 1/6) intravenously or 16 mg. (gr. 1/4) hypodermically, for relief of pain. Administration of penicillin in full dosage of 40,000 units every three hours is begun upon admission, to be continued without interruption until at least the fifth postoperative day.

A Levin tube is introduced and the gastric contents, chiefly air, are aspirated; under no circumstances, however, should any solution be introduced into the stomach for lavage.

Operation is usually performed under spinal anesthesia and consists simply of closure of the perforation. At operation, any material which may have collected in the pelvis, lateral colic gutters, or subhepatic space is sucked out to decrease the likelihood of postoperative intraperitoneal abscess formation. In past years it was customary to leave several grams of powdered or crystalline sulfanilamide in the abdomen; this procedure has been abandoned in favor of systemic administration of penicillin or sulfadiazine or both in full dosage from the time of admission until the danger of peritonitis or abscess formation is past. The abdomen is usually closed without drainage, although most surgeons prefer to leave a rubber dam drain in the wound down to the closed peritoneal layer for two days to discourage the development of wound infection.

**POSTOPERATIVE CARE.**—Postoperative care is similar to that following perforative appendicitis except that a Miller-Abbott tube is not used. The patient is returned to his room with orders for the gastric tube to be attached to a Wangenstein suction apparatus, morphine 10 to 16 mg. (gr.  $1/6$  to  $1/4$ ), to be given as needed for pain during the first day (not oftener than every four hours), position to be changed every two hours when awake, and deep-breathing exercises every hour and frequent leg exercises to be done. An oxygen tent is supplied if necessary and hourly carbon dioxide inhalations are ordered when advisable. Orders for penicillin with or without sulfadiazine are confirmed and a blood transfusion is given if the patient's condition is poor. Nothing is permitted by mouth for at least three days; the gastric tube is removed at this time if gastric and intestinal peristalsis are returning.

Fluid and nutritional intake, with added vitamins, is supplied by infusion for the first few days after operation; enough fluid is given to insure a daily total urinary output of 1,000 to 1,500 cubic centimeters. Usually 2,500 to 3,500 c.c. of fluid each day will prove sufficient. From 1,000 to 2,000 c.c. are given as protein hydrolysate (5 per cent) in dextrose (5 per cent) solution and the remainder as either normal salt or dextrose (10 per cent) solution. No normal salt solution is given for

twenty-four hours after operation; after this time the salt requirement is satisfied by 1 liter of normal salt solution daily plus an amount equal to one-half the quantity of fluid recovered from the stomach by aspiration. After removal of the gastric suction tube the patient is placed on the usual routine gastroenterostomy diet and is required to follow closely a medical regime for peptic ulcer after discharge from the hospital.

Complications following operative closure of a perforated peptic ulcer are frequent. Patients who are operated upon within six hours after onset of perforation recover generally without incident; if operation is delayed for from six to twelve hours, the postoperative course is more likely to be complicated. The mortality rate is a great deal higher if perforation occurred more than twelve hours before operation and an unfavorable outcome is likely in those in whom operation has been delayed for twenty-four hours or more.

In patients with active peptic ulcer, few pathogenic bacteria are present in the gastric contents. Closure of a perforated ulcer within the first few hours therefore is rarely followed by peritonitis. The acute peritoneal inflammation, however, may produce a temporary paralysis of the stomach and duodenum so that regurgitation of duodenal and jejunal contents may occur. If the perforation remains open for twelve hours or more, contamination of the peritoneal cavity by bacteria from the upper and even the lower small intestine is likely, with resulting generalized peritonitis. This complication is the commonest cause of death in these patients.

Other frequent postoperative complications include atelectasis or pneumonia, subphrenic space infection, pelvic abscess, and wound infection. Each of these possibilities must be considered in patients who show poor recovery following operation and the proper measures for diagnosis and treatment instituted. Rarely, temporary pyloric obstruction may develop as the result of residual inflammation in the region of the ulcer. Treatment consists simply of correction of hypoproteinemia by administration of blood transfusions and protein hydrolysate infusions with therapeutic doses of vitamins B complex and C, with continuation of antibacterial therapy in full dosage.

From time to time the suggestion has been made that subtotal gastric resection<sup>18</sup> rather than simple closure of the per-

foration will relieve the patient of symptoms and of the likelihood of further trouble with the ulcer. It is true that following simple closure, approximately 40 per cent<sup>17</sup> of patients will develop such symptoms as pain, bleeding, pyloric obstruction, or reperforation, but less than one-third of these will require subsequent operation rather than medical care alone. This number appears to be too small to warrant the added risk of primary gastric resection for acute perforated duodenal ulcer, even in selected cases. A better argument for primary gastric resection can perhaps be advanced for treatment of perforated gastric ulcer, which occasionally may be carcinomatous. The prognosis following resection of a perforated carcinomatous ulcer of the stomach is so poor, however, that it makes little difference whether resection or simple closure is performed.

### Vagus Resection

The value of vagus resection in the treatment of peptic ulcer is still undecided. Transabdominal section of the vagus nerves for ulcer had been attempted at various times in past years but without much success, probably because many fibers were left intact. With the introduction of intrathoracic vagus resection by Dragstedt<sup>18</sup> and the appearance of confirmatory reports by others,<sup>19,20</sup> it became possible to study the effects of total parasympathetic denervation of the ulcerated stomach. Vagus resection may be performed equally effectively by the transabdominal<sup>21,22</sup> or the transthoracic route.<sup>23</sup>

The purpose of the procedure is not so much to diminish the acidity of the gastric juice or to decrease the secretory response to meals but to abolish the continuous secretion of large amounts of gastric juice between meals and at night, when there is no food present to buffer the acidity of the secretion. Vagus denervation of the stomach also relieves the muscular spasm characteristic of active peptic ulcer. Prompt relief of pain, decrease of night secretion, and clinical healing of the ulcer follow operation in a high percentage of cases. Study of these patients has shown that the secretory response to injection of histamine is unchanged, although the sham meal no longer will stimulate gastric secretion. The effects of psychic factors such as worry, emotion, and nervous tension upon gastric secretion consequently are decreased, although normal gastric secretion following ingestion

of food continues. Normal sensations of hunger and nausea are still felt following vagus resection. The denervation, however, must be complete; if any fibers are left intact following division of the two large vagus trunks, the excessive continuous secretion of gastric juice will remain unchanged and the symptoms will continue. Section of the remaining fibers then may be followed by the desired decrease in secretion and symptomatic relief<sup>21</sup>

The chief disadvantage of the operation as a treatment for peptic ulcer is that in many cases gastric motility is too greatly decreased, with retention of food in the stomach for periods of six hours or more. While this effect improves somewhat with the passage of time, the delayed emptying and gastric dilatation present a difficult problem in management, neither change of diet nor use of drugs producing much corrective effect. Secondary gastroenterostomy may be necessary<sup>24</sup> in a high percentage of cases if not performed at the time vagotomy is done. Other untoward symptoms such as diarrhea or eructation of foul-smelling material may occur, or sensations of weakness, faintness, or gastric fullness may develop following ingestion of relatively small quantities of food. Several cases have been reported<sup>25</sup> in which unhealed ulcers have progressed to perforation, the complication being recognized with difficulty because of the lack of characteristic symptoms. Dragstedt and associates<sup>21</sup> report, however, that in their group of cases the clinical results have been so satisfactory and the complications so transitory and unimportant that this method of surgical treatment for peptic ulcer has very largely replaced all others. Other clinics have reported less satisfactory results; Walters and associates,<sup>22</sup> for example, state that in their experience the results of vagus nerve section are "inconstant, variable, and in most cases unpredictable." The place of this operation in treatment of peptic ulcer is not yet established but is still under debate.

In general, vagus resection for peptic ulcer has been found most useful in patients with early gastrojejunal ulceration following previous gastric resection or with acute inflammatory duodenal ulcer unusually difficult to remove surgically. In the former case, a gastrojejunal stoma is already present; in the latter case, simultaneous gastroenterostomy is advisable. Unless complementary gastroenterostomy is performed, vagotomy is strongly contraindicated in the presence of pyloric obstruction,

even of the slightest degree, because the operation itself tends to cause gastric retention and delayed emptying. Transthoracic vagotomy alone is not acceptable as treatment for gastric ulcer under any circumstances, because the thoracic approach will not permit inspection of the possibly malignant lesion. Transabdominal division of the vagus nerve filaments at the esophageal level, now preferred by most surgeons to the transthoracic procedure, may prove to be of value also as a supplement to subtotal gastric resection when acidity is high and stomal ulcer is expected. The greatest advantages of the abdominal approach<sup>21,22</sup> for vagotomy are that the lesion can be examined and simultaneous gastric resection or gastroenterostomy performed if necessary. Because the operation has been in use for only a relatively short time, it is not possible at present to be certain whether the effects are permanent or will prove to be only temporary.

Preoperative preparation is the same as for other gastric operations; when vagus neurectomy is planned, a Levin tube is introduced into the stomach before operation. The transthoracic operation is performed under intratracheal anesthesia with a high concentration of oxygen; aspiration of the tracheobronchial tree is performed before the patient leaves the operating room. The chest is closed without drainage. Pain in the region of the incision can be minimized by the injection of procaine (1 per cent) around the intercostal nerves near the necks of the ribs immediately above and below the incision; this procedure can be repeated later if necessary. If pleural fluid accumulates during the early postoperative period, it is removed by thoracentesis; if atelectasis develops, it is treated in the usual manner. Following a thoracic operation it is customary to allow the patient out of bed promptly, usually on the first or second postoperative day.

Transabdominal vagotomy is now generally preferred to the transthoracic procedure; postoperative care following the abdominal operation is much the same as that following any gastric surgical operation. Constant gastric suction drainage, begun before operation, is continued for at least five to six days postoperatively in all cases, and subsequent return to diet is slow and cautious. The patient should be followed for a long time until satisfactory gastric digestion and motility return. An



occasional patient will require gastroenterostomy to correct gastric retention following vagus resection. Close watch is kept for the occurrence of residual gastric retention for some months.

Gastric and small intestinal peristalsis can be increased temporarily following vagus resection by administration<sup>27</sup> of Urecholine, a parasympathomimetic drug, in doses of 5 mg. hypodermically or 10 to 30 mg. orally. The effects of the drug last for from thirty to forty-five minutes. Partial relief of troublesome symptoms in the late postoperative period can sometimes be obtained by a dose of 10 mg. given orally one-half hour before meals.

A clinical test has been developed<sup>28</sup> to determine if operative division of the vagus fibers to the stomach has been complete. The test is based on the fact that hypoglycemia produced by injection of insulin causes stimulation of the vagus secretory fibers, with prompt secretion of gastric juice. The test is performed during the preoperative period and again ten to fourteen days after operation.

The suggested procedure is as follows: Light diet (Sippy) is given the day before the test, with no food permitted after supper and no fluids after midnight. In the morning a Levin tube (14 French) is passed without the usual sips of water; all saliva secreted during passage of the tube and performance of the test should be expectorated by the patient rather than swallowed. When the tube has reached the stomach, all the gastric contents are aspirated with a syringe and the specimen is labeled accordingly. At this time a sample of blood is drawn for fasting blood sugar analysis. A dose of 15 units of regular insulin is slowly injected intravenously and the time is recorded. Because of the danger of hypoglycemic shock, the test should be conducted by a physician; a sterile solution of dextrose (10 per cent) should be prepared and ready for immediate injection if a hypoglycemic reaction should develop. Every fifteen minutes following injection of insulin the stomach contents are aspirated; the time and amount of collection and the presence or absence of bile and mucus are recorded. A sample of each specimen is labeled and kept for titration. With alternate specimens (every thirty minutes), a sample of blood is drawn for blood sugar determination and labeled with the time of withdrawal. The procedure is continued for two hours, resulting in the collection of nine samples of gastric juice, one collected before and eight after insulin

injection, and four samples of blood, one collected before and three after insulin administration. The free and total acid values are determined on each specimen of gastric juice.

The test is not reliable unless the blood sugar is depressed below 50 mg. per cent by the injection of insulin; if 15 units are insufficient, the procedure is repeated the following day with a dose of 20 units. If gastroenterostomy has been performed, regurgitation of duodenal contents into the stomach may occur and depress the acidity of the gastric juice; each specimen is examined for bile for this reason. The test performed before operation should be positive, showing a secretion of acid gastric juice in response to insulin; the test performed after vagus resection should be negative, showing no change in gastric secretion after administration of insulin. If the test is positive following operation, it is presumptive evidence that some few vagus fibers have remained intact. A single negative test, however, is not conclusive.

### Gastrostomy

When obstruction or acute inflammation of the esophagus is present, a gastrostomy is necessary for feeding purposes. If normal esophageal function can be expected after a period of a few weeks, temporary gastrostomy is performed; when the esophageal block or interruption is of a more long-standing or permanent nature, a permanent gastrostomy is made.

Fistulas, including gastrostomies, tend to heal if the tract is long or narrow and tend to remain open permanently if the entire tract is lined with epithelium. A *temporary gastrostomy* is made by introduction of a catheter, preferably of the Pezzer type with the tip cut away so as to leave a flange, into the stomach through a small incision; the catheter is brought out through the abdominal wall and is fixed by a single nonpenetrating suture to the seromuscular coat of the stomach and similarly to the skin. The catheter must remain in place constantly even after the retaining sutures have loosened; it should be taped securely in position as long as its use is necessary. If the catheter is removed between feedings or is allowed to remain out for more than a few hours, the gastrostomy channel soon becomes partially occluded by granulation tissue and scar forma-

tion, and reinsertion of the catheter becomes progressively more difficult. Even if the catheter is properly left in place and is removed only occasionally for cleaning, a gastrostomy of this type will not function satisfactorily after a few weeks have passed.

A gastrostomy of the *permanent* type is made either by drawing a portion of the stomach wall out to the skin surface and suturing it in position or by constructing a hollow tube from a full-thickness flap of stomach wall and fixing it to the skin. Such a gastrostomy channel is lined with mucosa all the way to the skin level and will remain patent for as long as it is needed. The catheter which is left in place at operation can be removed after four or five days when primary healing of the incision has occurred. After this time the tube is reinserted only for feeding and is then removed again. A gastrostomy of this type may shrink somewhat if the channel has been made too small, if the abdominal wound has been closed too tightly around it, or if infection and partial sloughing take place.

Feeding is carried out by vein for the first twelve to twenty-four hours. After this time, liquid diet may be given, preferably of the high protein, high carbohydrate, fat-free type (p. 72) with added vitamins. The feeding is introduced slowly by means of a funnel or a bulb syringe. Amounts of 100 to 150 c.c. are given every four hours for the first three to four days after operation, and the quantity is progressively increased according to the patient's tolerance until liquid meals of 600 to 1,000 c.c. each are given four times a day. Before feeding is begun aspiration is attempted to make sure that the previous meal has passed out of the stomach. When the simple protein-carbohydrate feeding is tolerated well, fat can be added (cream), as in the jejunostomy diet. As convalescence progresses, a properly balanced high caloric liquid diet, containing at least 2 Gm. of protein per kilogram body weight per day (twice the normal dietary protein intake), can be devised.

Leakage of food occurs most commonly from the temporary type of gastrostomy and can be minimized by clamping the tube and applying a snug dressing after each feeding. Leakage is less likely to occur if the feeding is introduced slowly and if the patient remains flat on his back for a short while after each meal.

Several types of permanent gastrostomy are made with a valve-like fold of gastric wall at the base to decrease the likelihood of leakage. •

### Congenital Hypertrophic Pyloric Stenosis

Preoperative and postoperative care in surgical treatment of this condition, which is seen only in infants several weeks old, is discussed in Chapter 9 (pp. 194 and 195).

### References

1. Maimon, S. N., and Palmer, W. L.: Gastric Cancer: Laparotomy, Resectability, and Mortality, *Surg., Gynec. & Obst.* 83: 480, 1946.
2. Counsellor, V. S., Waugh, J. M., and Clagett, O. T.: Report of Surgery of the Stomach and Duodenum for 1943, *Proc. Staff. Meet., Mayo Clin.* 19: 586, 1944.
3. Co Tul, Wright, A. M., Mulholland, J. H., Galvin, T., Barcham, I., and Gerst, G. R.: The Hyperalimentation Treatment of Peptic Ulcer With Amino Acids (Amigen) and Dextri-Maltose, *Gastroenterology* 5: 5, 1945.
4. Sweet, R. H.: Transthoracic Resection of the Esophagus and Stomach for Carcinoma, *Ann. Surg.* 121: 272, 1945.
5. Co Tul, Wright, A. M., Mulholland, J. H., Carabba, Y., Barcham, I., and Vinci, V. J.: Studies on Surgical Convalescence. I. Sources of Nitrogen Loss Postgastrectomy and Effect of High Amino-Acid and High Caloric Intake on Convalescence, *Ann. Surg.* 120: 99, 1944.
6. Abbott, W. O., and Rawson, A. J.: A Tube for Use in the Postoperative Care of Gastro-Enterostomy Patients, *J. A. M. A.* 112: 2414, 1939.
7. Hollander, F., Rosenak, S., and Colp, R.: A Synthetic Predigested Aliment for Jejunostomy Feeding, *Surgery* 17: 754, 1945.
8. Smith, F. H.: Total Gastrectomy; Report of 89 Cases, *Surg., Gynec. & Obst.* 81: 402, 1947.
9. Shapiro, A. L., and Robillard, G. L.: Morphology and Variations of the Duodenal Vasculature, *Arch. Surg.* 52: 571, 1946.
10. Rienhoff, W. F., Jr.: An Analysis of the Results of the Surgical Treatment of 260 Consecutive Cases of Chronic Peptic Ulcer of the Duodenum, *Ann. Surg.* 121: 583, 1945.
11. Jordan, S. M.: End Results of Radical Surgery of Gastrointestinal Tract as Seen by Gastro-Enterologist, *J. A. M. A.* 116: 586, 1941.
12. Berkman, J. M., and Heck, F. J.: Symptoms Following Partial Gastric Resection, *Gastroenterology* 5: 85, 1945.
13. Moore, F. D., Chapman, W. P., Schultz, M. D., and Jones, C. M.: Resection of the Vagus Nerves in Peptic Ulcer, *J. A. M. A.* 133: 741, 1947.

14. Heuer, G. J.: The Surgical Aspects of Hemorrhage From Peptic Ulcer, *New England J. Med.* 235: 777, 1946
15. Graham, R. R., and Tovee, E. B.: The Treatment of Perforated Duodenal Ulcers, *Surgery* 17: 704, 1945
16. Strauss, A.: Primary Gastric Resection for Perforated Gastroduodenal Ulcers, *Ann. Surg.* 120: 60, 1944
17. Werbel, L. W., Kozoll, D. D., and Meyer, K. A.: Surgical Sequelae Following Recovery From a Perforated Peptic Ulcer, *S. Clin. North America* 27: 95, 1947.
18. Dragstedt, L. R.: Vagotomy for Gastroduodenal Ulcer, *Ann. Surg.* 122: 973, 1945.
19. Moore, F. D., Chapman, W. P., Schultz, M. D., and Jones, C. M.: Transdiaphragmatic Resection of the Vagus Nerves for Peptic Ulcer, *New England J. Med.* 231: 241, 1946
20. Grimson, K. S., Baylin, G. J., Taylor, H. M., Hesser, F. H., and Rundles, R. H.: Transthoracic Vagotomy, *J. A. M. A.* 131: 925, 1947
21. Dragstedt, L. R., Fournier, H. J., Woodward, E. R., Tovee, E. B., and Harper, P. V., Jr.: Transabdominal Gastric Vagotomy, *Surg., Gynec. & Obst.* 83: 461, 1947.
22. Walters, W., Neibling, H. A., Bradley, W. F., Small, J. T., and Wilson, J. W.: A Study of the Results, Both Favorable and Unfavorable, of Section of the Vagus Nerves in the Treatment of Peptic Ulcer, *Ann. Surg.* 126: 679, 1947.
23. Moore, F. D.: Vagus Resection for Ulcer. An Interim Evaluation, *Ann. Surg.* 126: 664, 1947.
24. Grimson, K. S.: Discussion, *Ann. Surg.* 126: 699, 1947.
25. Weinstein, V. A., Colp, R., Hollander, F., and Jennerin, E. L.: Vagotomy in Therapy of Peptic Ulcer, *Surg., Gynec. & Obst.* 79: 297, 1947.

## CHAPTER 19

# SMALL INTESTINE AND APPENDIX

### Small Bowel

Most lesions of the small bowel which require operation produce obstruction, either partial or total, as the presenting symptom. The obstruction may be due to extrinsic causes such as (1) internal or external herniation through an abnormal or an abnormally large opening, (2) block by a band or area of adhesions, either congenital, acute, inflammatory, or fibrous, or, less commonly, (3) involvement by neoplastic tissue arising in adjacent structures. In other cases the obstruction is intrinsic, arising from acute or chronic intussusception, neoplastic disease, or an acute or chronic inflammatory state with either proliferative or fibrotic changes in the bowel wall; occasionally also obstruction of the small bowel may be due to a foreign body such as a swallowed object, a mass of vegetable material, a collection of parasites, or even a gallstone which has ulcerated through the gall bladder wall into the lumen of the small intestine.

The diagnosis and treatment of acute intestinal obstruction, both complete and incomplete, are discussed in another chapter; the management of chronic incomplete obstruction of the small bowel differs in some details. The symptoms of intrinsic lesions of the small intestine depend chiefly upon the production of a recurrent partial block in the lumen; the patient characteristically experiences periodic attacks of epigastric distress and ill-defined, poorly localized abdominal pain of a cramping nature, occasionally with nausea and vomiting and less commonly with abdominal distention. When inflammatory changes are present, as in the case of regional enteritis, the symptoms resulting from an acute intra-abdominal infection are added to the picture.

Much information can be gained by the proper use of x-ray studies. A plain erect roentgenogram will show abnormal accumulations of air in the small bowel as well as fluid levels, if present; a barium meal (gastrointestinal series) occasionally will

demonstrate the presence of an intrinsic lesion, although an x-ray series which appears normal does not rule out such a condition. The diagnostic value of the "string sign" in regional enteritis is well known. Caution is always necessary in the use of barium for diagnostic studies in patients who exhibit evidence of intestinal obstruction, either partial or complete. Barium can be administered by enema with safety since it can be evacuated spontaneously by the patient or recovered by irrigation. Barium administered by mouth is definitely dangerous in patients whose obstruction is of sufficient degree to cause abnormal retention of air, since the barium cannot be recovered and tends to accumulate at the point of obstruction. When partial obstruction is slight enough to be asymptomatic at intervals and no air is present in the small bowel on roentgenography, it is safe to administer barium by mouth for diagnostic study. If an appreciable degree of obstruction is present, however, barium is not needed to make the diagnosis and may occlude the remaining lumen and precipitate acute complete block.

**Preoperative Care.**—Complete intestinal obstruction requires immediate operation with a minimum of time spent in preparation. Partial block of the small bowel is less urgent and several days may be spent profitably in cleaning the bowel above the lesion. Recurrent attacks of obstruction, in which powerful peristaltic contractions occur, are accompanied by edema and inflammatory infiltration of the bowel. The intestinal wall in this state is soft and friable, and sutures are likely to tear the tissue and produce either small leaks or areas of necrosis and subsequent separation. Preoperative decompression for several days by means of constant gastroduodenal suction or the Miller-Abbott tube will empty the small bowel and reduce peristaltic activity, with improvement in local circulation and nutritional state. During this period a normal fluid and electrolyte balance is attained by means of infusions, and other measures are taken as indicated. When obstruction has not been present, preoperative suction is not necessary; administration of a nonresidue liquid diet for several days will keep the bowel at rest and prevent accumulation of intestinal contents.

Following operation the bowel is kept at physiologic rest until healing is advanced. Suction by gastroduodenal tube is

continued until normal peristalsis returns; if vomiting or gastric retention reappears after the tube has been removed, suction should be reinstituted immediately. Nonresidue liquid diet in small amounts is begun on the third or fourth postoperative day, after suction has been discontinued, and dietary intake is increased slowly thereafter. A soft low-residue diet is permissible by the sixth day and a light diet by the tenth, with gradual increase in the types and quantity of food allowed. It is generally unwise either to starve the patient too long or to increase the diet too quickly following resection and anastomosis of the small bowel.

The chief concern of the postoperative period is to prevent the development of ileus, which strains the suture line and interferes with circulation in the healing area. The most serious complications are peritonitis due to leakage or partial separation at the anastomosis and obstruction due to occlusion or kinking of the intestine in the region of operation. Occasionally, transient partial obstruction may develop due to edema at the anastomosis; either excessive fluid administration or nutritional deficiency (hypoproteinemia and avitaminosis) may be the cause. The patient is watched closely if signs of partial obstruction appear; gastroduodenal suction is instituted at once and serial x-ray films are made at intervals of two hours to note any evidence of progressive distention. When increasing accumulation of air or fluid appears in a loop of small intestine under these circumstances, prompt operation is necessary; such obstruction may be present not only at the anastomosis, but also in adjacent loops, fixed to the traumatized area by fibrinous adhesions.

### Enterostomy

Management of an enterostomy requires close attention and dependable nursing care. An external opening into the small intestine is made either as a means of supplying food to a debilitated patient who is unable to take sufficient quantities by mouth or, less commonly, as a decompressive measure to relieve back pressure in the intestine obstructed by mechanical causes or by paralytic ileus. The catheter, fixed into the intestine at operation, is attached to the skin at the



wound margin by a single silk suture passed only partially through the wall of the catheter without penetrating the lumen

Feeding by enterostomy is best done by means of an automatic drip apparatus of the type used for administration of aluminum gel in treatment of acute peptic ulcer. The nutritional mixture (p. 614) is given at a rate varying from 25 to 150 c.c. per hour, depending upon the requirements and digestive capacity of the patient. Care is necessary to insure that no air enters the bowel; the reservoir should not run dry and the enterostomy catheter should be clamped securely when feeding is interrupted or the apparatus is disconnected. Introduction of even a small amount of air into the intestine will produce discomfort and distention, interfere with peristalsis, and delay absorption. If the tube becomes blocked, gentle irrigation with normal salt solution through a bulb syringe will release the obstruction. Forceful irrigation is dangerous, especially during the early postoperative period before the enterostomy drainage tract is sealed off; excess pressure may force fluid into the peritoneal cavity or into the wound at this time. Small quantities of irrigating fluid are used to avoid distending the bowel and care is taken to prevent introduction of air. After twelve to fourteen days, if feeding is no longer required, the catheter can be removed and a snug petrolatum gauze dressing applied to prevent temporary leakage. If peristalsis is normal and no obstruction is present distally, the fistula will heal within several days with little drainage.

Enterostomy in treatment of obstruction is for drainage of accumulating intestinal contents rather than for feeding. In some cases it is performed as a last resort in a seriously ill patient when passage of a Miller-Abbott tube is impossible and spreading or generalized peritonitis is present. Although the procedure is a recognized one and is accepted as a means of draining the distended atonic small bowel in advanced paralytic ileus, it should not be performed unless all other methods of treatment have been given a thorough trial without success. On the other hand, if enterostomy for drainage is to be of value, it should not be delayed until all peristaltic activity has disappeared and the patient is moribund; if atonicity is complete, the fistula will empty only the drained loop of small bowel and nothing will be gained.

A draining enterostomy is a difficult nursing problem. As peristalsis returns, an increasing amount of intestinal fluid pours from the wound, digesting the edges of the incision and the surface of the abdomen and dislodging the enterostomy tube. Later, as the patient begins to take some food by mouth, the drainage thickens and becomes more profuse as the secretion of digestive juices is stimulated.

Large quantities of body water, electrolytes, minerals, and protein are lost in this way, and the patient is in danger of being drained of body fluid and nutritional reserves as he recovers from the ileus and peritonitis. Daily fluid loss and fluid intake are charted as accurately as possible; enough fluid is supplied by oral and parenteral routes to maintain normal hydration and to insure a daily urinary output of 1,000 to 1,500 cubic centimeters. Because a significant amount of salt is lost in the intestinal drainage, it is advisable to secure blood chloride determinations at frequent intervals. Protein feeding is of the greatest possible value in patients of this type; from 1 to 2 liters of protein hydrolysate solution (5 per cent) containing dextrose (5 per cent) can be given intravenously daily. The amount of salt present in the protein preparation should be ascertained and considered in calculation of daily sodium chloride intake; further requirements are met by infusion of normal or half normal salt solution. In general, the basal salt need does not exceed 4 to 6 Gm. daily; when necessary, this amount is supplemented by half normal salt solution (equal parts of normal salt solution and dextrose 5 per cent solution) in a quantity equivalent to the volume of drainage from the enterostomy. While salt replacement is highly important, the danger of administering excessive amounts, with resultant fluid retention and edema, usually is greater than that of supplying too little. These patients also develop anemia and hypoproteinemia rapidly, in most cases even before enterostomy is performed; transfusions of blood are given as needed and full doses of B complex and C vitamins are administered regularly.

After the enterostomy tube drops away, the intestinal discharge is collected in voluminous gauze dressings. Measures for protecting the skin (p. 659) are begun immediately after operation and continued without interruption; although it is scarcely possible to prevent damage to the abdominal wall, it should be kept at a minimum. Such an enterostomy is not

necessary after ten to fourteen days have passed, by this time, either the patient has succumbed or peristalsis is normal and regular. Spontaneous closure is desirable and occasionally occurs; in most cases, surgical repair is necessary and should be performed within two weeks or less, if possible.

### Appendix

Removal of the appendix during or after an attack of acute inflammation is followed by uneventful recovery in most cases. The mortality due to appendicitis has been decreasing steadily and progressively and is no longer high; fatalities are due to the complications of appendicitis rather than to the disease itself. While recognition and operative treatment of the average case of early acute appendicitis offers little difficulty when the inflamed organ is in its usual location, the clinical picture may be highly atypical and confusing when the appendix is situated behind the cecum or in the pelvis. The occasional occurrence of acute appendicitis in patients under treatment for other diseases should be remembered. A sudden attack of appendicitis may develop in an individual convalescing from a fracture or being treated for cardiac disease or diabetes as well as in a subject in otherwise normal health.

**Interval Appendectomy.**—Hospital care is simplest when the appendix is removed several weeks following an acute attack, after the inflammatory reaction has subsided completely. The usual routine preoperative studies are made, including examination of the heart and lungs, blood pressure reading, urinalysis, and hemoglobin determination. A tapwater enema is given the night before operation, a hypnotic is ordered if necessary, and nothing is allowed by mouth after midnight. On the morning of operation, a short-acting barbiturate is administered from one and a half to two hours preoperatively and morphine and scopolamine (or atropine) are given hypodermically forty-five minutes before operation.

Routine postoperative orders are left, including a narcotic for pain. A small enema of water (60 c.c.) and glycerin (60 c.c.) is safe and effective for encouragement of postoperative voiding and passage of flatus; large enemas and cathartics are withheld until after the sixth day. If a McBurney incision is used, it is safe to allow the patient to sit up or to stand by the bed to

void; even surgeons who do not subscribe to early ambulation usually permit use of a bedside commode in preference to catheterization in these patients. Traditionally, the sutures are removed from the incision and the patient is allowed out of bed seven days after appendectomy through a McBurney incision; early postoperative ambulation, however, is being more widely employed and has much to recommend it.

Return to a full normal diet is rapid. Sips of water are allowed after nausea disappears, surgical liquid diet is given after twenty-four hours, and soft diet is supplied as soon as desired. As a rule, regular diet is taken by the fourth or fifth day, although a patient who is allowed up promptly will regain his appetite even more quickly.

**Acute Appendicitis.**—Management of the patient with acute appendicitis without rupture is much the same, although operation is performed as an emergency procedure. The usual preoperative examinations are made, including total and differential white blood cell counts. Urinalysis is especially necessary in patients with acute appendicitis as an aid both to evaluation of general condition and to establishment of the diagnosis. Dehydration due to vomiting will produce urinary concentration and acidity; in advanced dehydration, keto-acids also are present. Occasionally, diabetic acidosis will produce a clinical picture resembling acute appendicitis, especially in children; examination of the urine will reveal the possible alternative diagnosis. In such a case, correction of the metabolic disturbance by administration of insulin, fluids, and sugar will confirm the diagnosis of diabetes or will serve as adequate preparation if appendicitis actually is present. When the patient has been vomiting or restricting the fluid intake, it is advisable in any case to administer by infusion before operation 1,000 c.c. of fluid, consisting of normal salt solution and dextrose (5 per cent) solution in equal parts. Gastric lavage is not necessary unless the patient has eaten a short time before or unless an accumulation of fluid is present in the stomach.

When free fluid is noted in the peritoneal cavity at operation, a smear is made and a culture taken to determine the predominant organisms; antibacterial therapy following operation is ordered accordingly. The use of microcrystalline sulfanilamide intraperitoneally after appendectomy was widespread for several

years but has been abandoned almost entirely (p. 284). Many surgeons still favor its use, however, and it probably does little or no harm if used sparingly. The practice of pouring a predetermined quantity of the drug (for example, 5 Gm.) into the area of operation is definitely unwise, since the solid mass of sulfanilamide acts as a foreign body and a tissue irritant, creating dead space, increasing exudation, and favoring the development of postoperative adhesions. If employed, the drug is sprinkled over the tissues sparingly to form a light frosting.

Although it is unnecessary to drain the peritoneal cavity following removal of an acutely inflamed appendix without perforation, it is a worth-while precaution to leave a small rubber tissue drain down to the closed peritoneal layer for two or three days to prevent the accumulation of infected exudate in the wound. Early removal of the drain is followed by prompt healing without additional scar formation, and a serious wound infection may be prevented. Postoperative intestinal paresis persists somewhat longer when peritoneal inflammation is present; if nausea and vomiting continue for more than twenty-four hours, a Levin tube is passed, the stomach is emptied, and suction is instituted for a day or two.

**Appendicitis With Perforation.**—Inflammation of the appendix is accompanied by the outpouring of a sticky sero-fibrinous or plastic exudate. Precipitation of fibrin strands then causes the formation of adhesions between the diseased appendix and the surrounding tissues, with partial or complete isolation of the infected organ from the general peritoneal cavity. In some cases, formation of adhesions may progress rapidly, with effective walling off of the appendix before perforation occurs; in others, inflammatory necrosis of the appendix develops so quickly that perforation takes place before fibrinous adhesions have formed. In favorable cases, therefore, the necrotic appendix will discharge into a closed area walled off by surrounding adhesions, while in others the infectious material pours into the free peritoneal cavity. If localization by adhesions is incomplete when perforation occurs, the resulting peritoneal infection will spread beyond the ileocecal region, although at a slower rate than if no adhesions were present. Spreading peritonitis is characterized by extension of the zone of pain, tenderness, and rigidity in the lower abdomen and increase in the systemic effects of the disease.

An outpouring of fibrinopurulent exudate occurs as the infection extends, adjacent bowel loops become plastered together, and pockets of exudate collect between the intestinal coils. If the infection is sufficiently virulent, paresis of the inflamed small bowel occurs and the inflammatory process may progress quickly to generalized peritonitis. When body defenses are adequate, localization will occur with formation of pockets of pus in the region of the appendix, the cecum, the prerectal pouch, or the subphrenic spaces (p. 445). The retrocecal appendix is walled off from the general peritoneal cavity by virtue of its position.

Because of the danger of peritonitis, immediate emergency operation is mandatory in every case of acute appendicitis, whether or not perforation has taken place, unless a definite palpable mass is present and there is no evidence of spreading peritonitis. If the presence of a mass is probable but not positive, immediate operation is performed; delay is permissible only if localization and abscess formation are definite and unmistakable.

After removal of a recently ruptured appendix, the peritoneal cavity may be closed without drainage, although many surgeons prefer to use drains routinely if perforation has occurred. As a rule, drainage of the peritoneal cavity is employed when an abscess cavity has formed, when necrotic tissue or an unremoved appendix is left behind, or when leakage from the bowel is possible following operation. The incision, however, is never closed tightly following removal of a suppurative or perforated appendix. A small rubber tissue drain is left down to the closed peritoneum for several days to prevent accumulation of infected exudate under tension, or the peritoneum and fascia may be closed tightly, sutures being placed in the skin and subcutaneous tissue but left untied<sup>1</sup> for forty-eight hours. The usual postoperative measures are instituted, including gastro-duodenal suction and chemotherapy.

**Appendical Abscess.**—Appendicitis with localized abscess is generally treated conservatively during the early stages. The mass palpable in the right lower quadrant in these patients at first consists of acutely inflamed omentum, loops of bowel, and appendix matted together by fresh adhesions; if these are separated at operation, contamination of the peritoneal cavity by thin, highly infectious pus may occur or the bowel wall may be torn open. As the disease progresses, the limiting adhesions

become more dense and the area of inflammatory necrosis becomes liquefied; operation at this stage will permit drainage of the pus without contamination of the peritoneal cavity.

Most surgeons prefer to delay operation, therefore, if a well-defined mass is present<sup>2</sup> in the appendical region of a patient seen for the first time several days after onset of acute appendicitis. Complete bed rest is ordered and constant suction drainage is instituted by gastroduodenal or Miller-Abbott tube. The proper chemotherapeutic and antibiotic drugs are given parenterally in full dosage (p. 448) and fluids are supplied by infusion, with transfusion as indicated. The patient is watched closely during this time and the clinical course followed with care; examination of the mass, however, should be performed with the utmost gentleness. Rectal examination is made at intervals to detect spread of infection to the prerectal space.

Such a mass may regress, with coincidental clinical improvement; or it may grow firmer and more sharply defined, the general evidence of sepsis remaining undiminished; or it may rupture into the general peritoneal cavity, with spreading peritonitis. Extension of the infection to other areas of the abdomen may occur (Fig. 44) or the abscess may erode into the bowel, drain spontaneously, and subside.

Further treatment depends upon the clinical course. If the abscess regresses steadily and the evidences of sepsis decrease, operation is postponed for several weeks or months, until the inflammation has subsided completely. In some cases, the abscess will remain stationary or will increase in size and grow firmer and more tender; in such instances the patients will show no clinical improvement and may become more toxic, the temperature, pulse rate, and white blood cell count remaining elevated or rising. Such an abscess is drained without difficulty through a muscle-splitting incision, approaching the peritoneum laterally to avoid contamination of the abdominal cavity. The abscess is opened through its lateral aspect, the contained pus is sucked out gently, and one or two cigarette drains are placed down to the abscess cavity. These drains are removed after six to eight days and a small catheter is inserted to the bottom of the pocket to insure granulation from below upward.

If operation is undertaken during the earlier stages of abscess formation, little pus may be found, fresh adhesions may be broken, and pressure of the drains is more likely to cause formation of a fecal fistula. Many surgeons feel, however, that delay is dangerous and that acute appendicitis always requires immediate operation,<sup>3</sup> no matter at what stage the patient is first seen. In any case, a ruptured appendix that is treated by simple drainage must be removed by elective operation at a later date after all inflammation has subsided.

Postoperative care is much the same in localized or spreading peritonitis as in generalized peritonitis (p 446). Constant suction drainage is instituted promptly by Miller-Abbott or gastroduodenal tube. The tube is passed before operation to permit aspiration of air swallowed during and after the procedure and is removed only after effective intestinal peristalsis has returned. Oxygen is administered by nasal catheter for one or two days, transfusions of blood are supplied in sufficient quantity to maintain the hemoglobin and hematocrit at satisfactory levels, and enough fluids are supplied by infusion to insure a normal urinary output. Penicillin and sulfadiazine are given parenterally in full dosage (p. 448). Close attention to detail is necessary; urinary retention is likely to occur in these patients and atelectasis and bronchopneumonia are not infrequent. Intestinal paresis due to infection, mechanical block by adhesions, residual abscess near the cecum, collections of pus in the cul-de-sac or subphrenic spaces, and fecal fistula, in addition to other less characteristic complications such as thromboembolic disease, may develop.

Continued fever and leucocytosis without evidence of pus in the peritoneal cavity may be due to pelvic abscess or subphrenic space infection. Little discomfort may arise from either complication, although the patient shows increased toxicity. Neither abscess can be palpated through the abdomen, although a pelvic abscess may cause some distention, doughy resistance to palpation, and suprapubic tenderness. As a cul-de-sac abscess develops, repeated rectal or vaginal examination will reveal tenderness and an increasing boggy or firm induration; a discharge of pinkish mucus may be evacuated at intervals from the rectum or may be found on the examining finger. In many cases the tone of the sphincter is decreased. Such abscesses often



subside spontaneously under chemotherapy and supportive treatment; others will require incision and drainage after softening develops. The cul-de-sac abscess is opened by insertion of the tip of a pair of long curved scissors passed along the gloved finger either in the rectum or the vagina. Subphrenic space infections are drained extraperitoneally by the appropriate incision.

Organizing fibrinopurulent exudate may produce adhesions with mechanical intestinal block at any time from the fourth day after operation throughout the remaining years of the patient's life. While intestinal obstruction due to postoperative adhesions is not difficult to diagnose in itself, it presents a highly confusing and poorly defined clinical picture when associated with local or spreading peritonitis and paralytic ileus following removal or drainage of a perforated appendix. As previously stated (Chapter 14), postoperative paralytic ileus is continuous from the day of operation and is unaccompanied by colic; mechanical intestinal obstruction begins several days after operation, usually after an early favorable response has occurred and peristalsis is returning. Repeated auscultation and x-ray examination of the abdomen are necessary when there is any suspicion or possibility of mechanical obstruction after operation.

Suppurative pylephlebitis develops following discharge of infected thrombi from the appendical vein into the portal system and is characterized by sudden increase in toxicity, with chills, fever, and septicemia. Multiple liver abscesses develop and the course usually is rapidly downhill, the patient succumbing to the overwhelming infection. This complication is much less common since the introduction of the sulfonamide and antibiotic drugs, which have not only reduced its incidence, but also have proved therapeutically effective in occasional cases.

**Perforative Appendicitis With Generalized Peritonitis.**—Recovery from generalized peritonitis can scarcely be expected if a continuous leak is present and infective material drains steadily from the bowel into the peritoneal cavity. Patients who enter the hospital with fully established generalized peritonitis, however, are not acceptable operative risks, and several hours must be spent in improving their condition. Operation, when undertaken, is confined to the least taxing procedure possible; the appendix is removed if possible but is left behind

if its removal would be difficult or dangerous. In either case, one or two cigarette drains are inserted down to the area of rupture. Unless the patient is moribund, adhesions form around the drains and a fecal fistula may develop, with discharge of the purulent drainage out of the wound rather than into the abdomen. Recovery of the patient, however, depends also upon institution of the proper supportive measures, with the closest possible medical and nursing care. The diagnosis and treatment of generalized peritonitis is discussed in Chapter 14.



Fig. 64—A sump drain as used in generalized peritonitis. The drain is placed in the pelvis, the open end of the outer tube is not covered by the dressings but simply by a thin gauze pad. A wire screen fixed around the tube prevents its displacement but does not interfere with free entrance of air into the tube. In actual practice the bottle and motor are on the floor. (From Burnett, Rosemond and Caswell. *S. Clin. North America* 24:1316 1944, W. B. Saunders Co.)

Use of a "sump" drain in appendical peritonitis has been advocated by Burnett and associates,<sup>4</sup> who remark that ordinary drainage methods cause formation of dense adhesions with the danger of mechanical intestinal obstruction and are ineffective, purulent exudate overflowing from the wound only after the entire tract has become filled to the top. The sump drain consists of a metal suction tube within a perforated metal sheath, introduced through the incision to the deepest portion of the area to be drained. The advocates of the method, who have used it in a large series of cases, state that it removes pus as fast as

it collects, by suction from the bottom of the cavity rather than spillage from the top, that frequent changes of dressing are unnecessary since pus does not overflow from the wound, and that very few intra-abdominal adhesions develop, with correspondingly less danger of secondary intestinal obstruction.

The employment of this method of drainage is illustrated in Figs. 64 and 65. After the usual preoperative measures

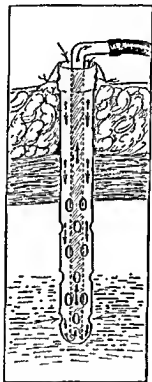


Fig. 65.—Diagram of the sump drain. Note impossibility of direct suction on bowel or omentum provided there is a free airway between inner and outer tube. Note fishmouth end of inner tube to avoid sealing. (From Barnett, Rosemond, and Caswell, *S. Clin. North America* 24:1316, 1911, W. B. Saunders Co.)

have been taken, a McBurney incision is made and the long tube is passed deeply into the cul-de-sac by the operator's left hand, guided by the gloved right index finger inserted into the rectum through the anus from below. When the tube is in place,

it is anchored to the skin with a single suture placed by the assistant, who has avoided contamination. Subsequent general measures include chemotherapy, gastroduodenal or Miller-Abbott tube suction drainage, blood transfusion, parenteral fluids, and morphine as indicated.

Proper management of the apparatus is not difficult but requires an understanding of its principles of operation. The outer tube serves as a protective sheath for the suction tube and prevents it from being blocked by omentum or bowel. Since a free flow of air is necessary to maintain suction, the open upper end of the outer sheath is allowed to project slightly above the dressing and is covered with a sterile thin aluminum screen to prevent occlusion or contamination by the bedclothes. Function of the sump drain depends on free circulation of air into the projecting open upper end of the larger tube; it must not be blocked at any time.

The integrity of the system can be tested by clamping the tube between the suction tip and the motor; the vacuum gauge needle will promptly rise above zero and the motor will labor audibly. If the inner (suction) tube of the system becomes blocked with exudate, the same effect is produced; the sound of the motor becomes strained, the gauge needle rises, and no effect is produced by clamping the tube. When blocked, the inner tube is removed, cleaned aseptically with sterile water, and replaced. Blocking of the perforations in the outer tube occurs after the exudate becomes thick and fibrinous, and a smaller amount is recovered by suction. Since cleaning and reinsertion of this tube is not possible, the motor is shut off, the fixation suture is clipped, and the entire drain is removed gently by a twisting motion. A small catheter is introduced into the drainage tract to allow healing from the bottom.

### References

1. Collier, F. A., and Valk, W. L.: Delayed Closure of Contaminated Wounds; Preliminary Report, *Ann. Surg.* 112: 256, 1940.
2. Ochsner, A., and Johnston, J. H.: Appendical Peritonitis, *Surgery* 17: 873, 1945.
3. Chenoweth, A. I.: Appendical Abscess, *Surgery* 11: 702, 1943.
4. Burnett, W. E., Rosemond, G. P., and Caswell, H. T.: The Use of the "Sump" Drain in Peritoneal Infection, *S. Clin. North America* 24: 1316, 1944.

## CHAPTER 20

### LARGE BOWEL

Successful outcome of a surgical procedure upon the large bowel requires accurate evaluation and well-planned management of the patient as well as skillful performance of the necessary operation. Most disorders of the colon that require surgical correction are chronic in nature and slow in development. As a consequence, significant alterations may occur in the patient's nutritional balance and general condition before the local manifestations of the lesion have become sufficiently marked to indicate its presence. Surgery of the colon, moreover, is attended by a relatively high mortality rate because of certain anatomic and physiologic characteristics of this portion of the gastrointestinal tract which are inherently unfavorable to the successful performance of operative procedures.

#### Ulcerative Colitis

Mild cases of ulcerative colitis usually are managed satisfactorily by conservative methods, although surgical procedures are necessary<sup>1</sup> in a large proportion of moderate to severe cases. Terminal ileostomy is performed for the diversion of the fecal stream when the colitis is severe and progressive in nature, and the operation is done early in the course of the disease rather than after deep-seated pathologic changes or serious complications have developed. If the severity of the condition abates following this procedure and the patient regains normal health, the divided ileum can be reanastomosed after a proper interval in occasional cases. When the colon is extensively diseased or when sufficient improvement does not occur following ileostomy, complete colectomy in two or more stages is usually the only remaining resource of the surgeon. Although the mortality of this operation is relatively high, it is at present the only means by which intractable ulcerative colitis can be cured.

The administration of succinylsulfathiazole (sulfasuxidine) and phthalylsulfathiazole (sulfathalidine)<sup>2</sup> has been reported to produce definite clinical improvement in a large percentage of

patients with acute and chronic ulcerative colitis. While these drugs cannot be expected to cure colitis of this type, they will effect clinical remission or marked improvement in the condition of the diseased colon in many cases if administered over a period of several months. As a result of the improvement in general health, the patient becomes a more acceptable surgical risk. There appears to be little difference in effectiveness of the two drugs. Streptomycin and penicillin appear to be of less value in ulcerative colitis than the appropriate sulfonamide drugs.

For a period of at least seven to ten days before operation, in any case, the patient receives either 3.0 Gm. of succinylsulfathiazole or 1.5 Gm. of phthalylsulfathiazole four times daily, continuing to the day of operation. Enemas are unnecessary; clinical improvement in most cases is accompanied by diminution of diarrhea and loss of blood. Although small retention enemas of tannic acid (0.5 per cent) or of starch and opium were formerly given to reduce mucosal bleeding, it is probable that such irrigations do little good and may provoke further irritation of the inflamed mucosa. Even the preparatory enema customarily given on the night before operation is omitted.

These patients are almost always poor operative risks and characteristically exhibit varying degrees of advanced malnutrition, dehydration, anemias, avitaminosis, and protein deficiency as a result of their intractable diarrhea, loss of blood, and prolonged dietary restrictions. Before any operative procedure can be undertaken, a thorough general physical examination is performed and laboratory studies are made, including urinalysis, complete blood count and determination of the plasma protein, carbon-dioxide combining power, chloride, and urea levels. Transfusions of blood are administered until the red cell count and hematocrit approach normal. A low-residue soft diet, high in caloric value and in carbohydrate and protein content, is prescribed. Vitamin concentrates, particularly A, B complex, and C, are administered in full therapeutic doses. Restoration of depleted body proteins can be expedited by addition to the diet of frequent intermediate nourishments containing 1 or more ounces of skim milk powder, milk protein concentrate, or even pure protein hydrolysate. When necessary, protein hydrolysate solutions can be given intravenously, together with dextrose, and will prove to be effective in restoring a positive nitrogen balance.

Dennis<sup>3</sup> advocates the administration of 2 to 3 liters of dextrose (20 per cent) intravenously during the twenty-four to thirty-six hour period immediately preceding operation; crude liver extract and parenteral vitamin preparations also can be added to the infusions. Tincture of opium or paregoric may be used to decrease the diarrhea.

These measures usually cause a rapid improvement in the patient's general condition and are continued until the peak of improvement has been reached. The indicated ileostomy may be performed at this time with much more likelihood of success than if preparation is minimal in extent. If blood loss per rectum is severe, however, immediate operation may be required almost as an emergency measure. In such a case, transfusions of blood are given, a gastroduodenal tube is passed just before operation, and a Wangenstein suction apparatus is connected immediately following operation. Aspiration is rarely necessary for more than three days after operation but is of value in minimizing small bowel distention and gastric retention during this time.

After operation, evidences of shock are watched for closely, and blood transfusions are administered if any signs suggestive of impending collapse appear. The usual postoperative regimen is followed. Surgical liquids are permitted after twenty-four hours and a soft low-residue diet after two days. Full therapeutic doses of vitamins B complex and C are continued, and blood transfusions are given routinely. Added protein is supplied by intermediate nourishment during convalescence and after discharge from the hospital.

During the immediate postoperative period, the ileal discharge is thin and watery and can be drained satisfactorily through a rubber tube. Since it is unsafe to leave the ileum clamped for even a few hours, a flanged tube (24 to 28 French) is inserted not more than one inch into the proximal ileal stump at operation and tied snugly with a purse-string suture. The ileal stump should project at least one and a half inches beyond the abdominal wall. The free end of the tube is attached to a Wangenstein constant suction apparatus and gentle suction is applied. Suction of this type will function effectively for only three or four days after operation, while the ileal drainage is thin and fluid. When the drainage thickens, the catheter is replaced

with a larger rubber tube and suction is supplied by means of a portable electric suction pump or a suction device operated by running water. A portable hand-operated apparatus has been described by Stone and Roddenbery<sup>4</sup>; the constant suction device reported by Lium<sup>5</sup> also is said to be effective and satisfactory. In most cases, suction drainage can be maintained without leakage for five days, by which time the wound has healed and an ileostomy bag (Koenig-Rutzen) can be fitted. This type of bag fits snugly around the ileal stump and is cemented to the skin at the base of the ileostomy, preventing leakage or excoriation.

Leakage from the ileostomy immediately after operation presents a problem difficult to manage. Every effort should be made to prevent skin irritation from beginning, for it is very difficult to keep the raw and excoriated area from spreading and progressing under the influence of the ileal tryptic juices once the process has begun. The consequent pain is severe and continuous, and constant nursing care becomes necessary. The danger of skin excoriation following ileostomy is great enough to justify the institution of protective measures routinely in all cases. Many methods of skin protection have been tried and none has proved dependably effective. In most cases the region of the stoma is coated thickly with aluminum paste or with kaolin in oil. If the aluminum paste will not adhere to the skin, the area is first cleaned thoroughly with ether or benzine and coated lightly with compound tincture of benzoin or liquid adherent. Aluminum powder dusted thickly over a moist application of tincture of benzoin may prove even more satisfactory. Ordinary rubber cement applied in several coats to the thoroughly dried unbroken skin usually works well, if the patient shows skin sensitivity to this preparation, the cement used in conjunction with the Padgett dermatome may be substituted. If a liquid adherent or cement is applied in several successive coats to the normal skin, a tough protective layer is formed that is resistant to the digestive juices. Some surgeons advocate the use of a sheet of rubber dam which is cut to cover the skin up to the base of the ileostomy and to extend well out over the abdomen and fixed by means of liquid adherent or rubber cement over the entire skin area to be covered. This type of protective dressing is effective but must be inspected frequently and changed at least once daily to prevent penetration



of ileal juices beneath it. Other waterproof coatings, such as vinylite resin, have been suggested. Oil or ointment dressings, which tend to macerate the skin, are less satisfactory than dry applications.

If the ileostomy stump projects well above the skin, a layer of flat gauze can be applied to the abdomen, then a sheet of rubber dam cut to fit closely around the protruding bowel, and then another layer of flat gauze and colostomy dressings. The sheet of rubber protective will decrease the amount of drainage which soaks through the dressings to the skin. If skin maceration and excoriation develop, local protective applications will not adhere and will be of little value. Under such circumstances, powdered casein or even skim milk powder can be applied thickly to inactivate the digestive juices which seep past the sheet of rubber protective; the dressing is changed frequently during the day.

Loss of body water and salts occurs rapidly during the period immediately following the establishment of an ileostomy, as a result of the continuous discharge of large quantities of intestinal fluid. Unless replacement therapy is carried out on a quantitative basis, dehydration and hypochloremia may develop. The intestinal contents lost by drainage are estimated and charted as accurately as possible and repeated studies are made of the blood chloride and serum protein levels. Because a large amount of sodium chloride is lost through ileostomy drainage, a correspondingly increased amount of normal or half normal salt solution in combination with dextrose is given intravenously to these patients until they are able to take a satisfactory diet. As much fluid, salt, and dextrose are given as necessary to keep the urinary output at the optimum level and to maintain the blood chlorides and carbon-dioxide combining power within the normal range. Parenteral administration is not necessary, of course, if the patient is able to take sufficient food and fluid by mouth.

After the patient has recovered from the effects of the operative procedure and the ileal discharge has become thick, a suitably constipating diet with restricted fluids may be instituted (Appendix.) Within two or three months the discharge has usually become more solid, and the patient is able to resume his customary activities. At best, a patient with a terminal ileostomy

will have from three to six bowel movements a day, but the rapid gain in weight and general health after operation may be little short of amazing.

If the disease is so far advanced that colectomy is considered necessary, an interval of six months should be allowed to enable the patient to regain strength.

### Neoplasms of the Colon

Malignant disease of the colon characteristically produces definite symptoms of altered bowel function. These changes may be so mild in nature and, although always progressive, may develop so insidiously that the patient, unaware of the gravity of the symptoms, may not seek medical advice until a year or more after appearance of the first evidences of the disease. In many cases, the patient will have already had a hemorrhoidectomy performed for rectal bleeding, while a carcinoma at a higher level has been permitted to progress unchecked because of lack of proper diagnostic investigation. Every patient past middle age who has a persistent alteration of bowel function or rectal bleeding, no matter how slight, should have a complete investigation for possible carcinoma of the colon. In many cases digital examination alone will reveal the lesion; in others it can be visualized by proctoscopic examination and confirmed by biopsy. If these examinations are negative, a barium enema is made, the roentgenologist being requested to introduce no more barium than is necessary to establish the location of the tumor, if present.

Although the operative procedures employed for removal of a carcinoma of the colon vary according to the personal preferences of the surgeon, the principles governing preoperative preparation and postoperative care are universally the same. Choice of the most appropriate operation depends upon several factors; for example, the general condition of the patient, the presence and degree of intestinal obstruction, the type and location of the lesion, and the presence of metastases and of local invasion.

**Preparation for Operation.**—Since carcinoma of the large bowel is commonest in the upper age groups, the physical examination of the elderly patient should include a thorough

search for signs of accompanying disease in the respiratory tract and for indications of decreased cardiac reserve or impaired renal function. The magnitude of the operation is such that a severe drain is placed upon the physical resources even of an individual in good condition, *the patient therefore must be brought quickly into the best possible condition before surgery is attempted.*

Dehydration, malnutrition, and anemia commonly occur in association with carcinoma of the colon, particularly of the right side. Restoration of fluid and electrolyte balance is accomplished by means of infusions of normal salt and dextrose solutions in the proper proportions by vein and large quantities of water and fruit juices by mouth. Fluid intake and output must be charted with accuracy during the entire hospital stay and a normal balance maintained. The depleted protein and carbohydrate stores of the body are renewed by means of a low-residue soft diet, high in caloric value (3,000 to 4,000 calories) and supplemented by intermediate nourishments high in protein content.

Repeated transfusions of blood should be given until the red cell count and hemoglobin values are approximately normal and the plasma protein concentration reaches 6.5 Gm. per cent. Vitamin concentrates (especially B complex and C) are given routinely in full therapeutic doses from the time of admission to the day of departure. X-ray studies for lesions of the large bowel are done entirely by barium enema. As in the case of small intestinal obstruction, no barium is given by mouth to patients with potentially or actually obstructive lesions of the colon, barium may accumulate proximal to the lesion and solidify into hard rocklike masses that will cause complete obstruction and interfere with operative procedures.

The changing trends in surgery of the colon have kept pace with the advancement in knowledge of anatomy and physiology of the large bowel. The earliest operations for carcinoma of the colon were performed as resections with immediate open anastomosis, but the mortality at that time was prohibitively high. The multiple stage operation advocated and popularized by Mikulicz therefore came into wide favor because of its much greater safety and, with certain modifications (obstructive resection), is still considered by many authorities as the safest and best procedure<sup>6</sup> for general use. However, because of the dis-

advantages of this operation, which requires open colostomy, prolonged hospitalization, and additional surgical procedures, the use of resection with primary anastomosis was never entirely abandoned. Improved techniques of primary anastomosis, with restoration of continuity without opening the bowel lumen, were developed and modified until methods were perfected<sup>7,8,9</sup> which gave results at least as good as those obtained with the generally safer but more troublesome multiple-stage obstructive resection. In still more recent years the use of intestinal antiseptics such as succinylsulfathiazole (sulfasuxidine) and phthalylsulfathiazole (sulfathalidine) has made open anastomosis<sup>10,11</sup> of the colon a safe procedure, perhaps as safe as closed or aseptic anastomosis; the danger of postoperative peritonitis or of wound infection from contamination at the time of operation is no longer a prohibitive one. Finally, with the widespread use of newer methods of nutrition and the administration of blood, plasma protein, hydrolysates, and vitamins in accordance with physiologic requirements, it has become possible to improve the condition of even aged or cachectic patients to such an extent that prolonged and difficult operations can be undertaken with safety.

The plan of preoperative preparation to be followed for cleansing of the colon before surgical removal of a carcinoma varies according to whether the tumor is causing obstruction of the bowel.

**WITHOUT OBSTRUCTION.**—If the lesion is not causing significant obstruction, the colon can be cleaned out effectively by mild catharsis and enemas. The patient is given  $\frac{1}{2}$  ounce of magnesium sulfate or Rochelle salt in the morning and an enema that night. The administration of an intestinal antiseptic drug is begun the same day, either sulfasuxidine in amounts of 3.0 Gm. four times daily or sulfathalidine in amounts of 1.5 Gm. four times daily for seven to ten days. The combination of measures of this type with administration of large quantities of fluids and a low-residue high caloric diet will assure the surgeon of a clean, empty, and properly prepared bowel at the time of operation. In general, sulfasuxidine and sulfathalidine are equally effective in clearing the colon of bacteria; either drug will reduce the coliform organisms in the large bowel and in the feces to an almost negligible number.<sup>12</sup> If the patient's cooperation can be de-

pendent upon, this period of preparation can be carried out at home. Following sulfasuxidine therapy, the patient's stools become soft, scanty in amount, and odorless, the use of an enema before operation is unnecessary. Sulfathalidine is equally satisfactory in this respect; the stools are decreased in quantity but become firm and even constipated. An enema therefore is advisable twenty-four hours before operation is performed, to insure proper emptying of the colon. Sulfathalidine is preferable for preoperative preparation of patients who have diarrhea, because of its constipating effect; it is more suitable also if cathartics or enemas must be used concurrently for any reason. Streptomycin also is effective in reducing the bacterial count in the large bowel before operation; for this purpose, it is given by mouth in a dose of 0.5 Gm. every four to six hours for two to four days immediately preceding operation. Some surgeons,<sup>6,7</sup> however, do not use intestinal antiseptics, preferring to cleanse the bowel by means of catharsis and flushes.

Any barium remaining in the colon following x-ray studies must be removed by enemas before operation. The material that remains distal to the site of the tumor can be washed out without difficulty, but the barium suspension which has passed beyond an incompletely obstructing tumor and collected above it may be difficult to remove. A fluoroscopic examination or a plain x-ray picture must be made the day before operation to reveal whether the colon is entirely empty; if an appreciable amount of barium is still present, operation is delayed until the bowel has been washed clean.

Current opinions differ concerning the necessity for routine colostomy proximal to the area of anastomosis with resection of a portion of the colon. Much depends, of course, on the location of the anastomosis. In conjunction with removal of the right colon and union of the terminal ileum and transverse colon, proximal surgical decompression is unnecessary, whether the operation is done in one or two stages. Whipple<sup>12</sup> has demonstrated that preoperative introduction of a Miller-Abbott tube down to the lower ileum in such a case not only facilitates performance of the operation, but also prevents dangerous postoperative distention of the ileocolic anastomosis. Simple gastroduodenal suction is a satisfactory substitute when a Miller-Abbott tube cannot be passed.

With respect to proximal colostomy with colonic anastomoses distal to the right colon, opinions are less in agreement. Most surgeons maintain that if there has been no obstruction and the bowel has been prepared properly for operation, surgical decompression is unnecessary and the institution of gastro-duodenal or Miller-Abbott tube suction drainage is sufficient, whether closed (aseptic)<sup>7,8</sup> or open<sup>10,11</sup> anastomosis is performed. Others believe that *complementary colostomy* is advisable, a small catheter being sutured at the time of operation into the normal colon several inches above the area of anastomosis (Maes) or into the cecum. Such a colostomy adds little to the operating time and heals spontaneously as soon as the catheter has served its purpose and is withdrawn after six to ten days. *Preliminary colostomy*, performed either by suturing a tube into the cecum<sup>14</sup> or by transverse colostomy from eight to twelve days before resection of the tumor, has also been advocated as the safest plan to follow if primary anastomosis is contemplated. This measure, however, is being abandoned<sup>14</sup> because recent improvement in methods of supportive care and antibacterial treatment have made it unnecessary. Preliminary colostomies in some cases must be closed surgically at a later date so that the entire procedure may require three operations, with increased hospitalization and prolonged convalescence. When a nonobstructing tumor of the bowel is removed by obstructive resection, obviously no proximal colostomy is necessary.

**WITH OBSTRUCTION.**—Preoperative preparation is complicated considerably if the lesion is causing obstruction of the colon.

The ileocecal valve, which projects slightly into the lumen of the cecum and is partially covered above and below by transverse mucosal folds, permits passage of fluid into the colon from above but becomes flattened and occluded when the pressure within the cecum rises, effectively preventing reflux of retained fluid or gas into the ileum. Existence of an obstructive lesion distal to the ileocecal valve therefore transforms the proximal portion of the colon into a closed loop. Pressure within the colon rises rapidly as fluid and gas are poured into the cecum by ileal peristalsis, so that complete obstruction of the colon is a surgical emergency. As the pressure increases, the bowel distends, the muscular coats become overstretched and atonic, and the venous

drainage is impaired. Congestion of the veins follows, edema and anoxia add to the physiologic damage, and areas of actual gangrene may develop. These changes are present also to a lesser degree if the obstruction is partial in nature rather than complete.

Since the obstructed portion of the colon is greatly distended, swollen, and edematous, sutures are likely to cut through the soft wet bowel wall. For this reason and also because there is a marked difference in diameter between the obstructed bowel above the lesion and the unobstructed bowel below, neither resection of the tumor-bearing area nor anastomosis can be done with ease or safety at this time but must be postponed for ten to fourteen days following relief of obstruction. Decompression is effected by establishment of a colostomy at some point between the ilcoecal valve and the site of obstruction (Fig 66), preferably far enough above the lesion to avoid interference with freedom of resection and anastomosis at a later date.

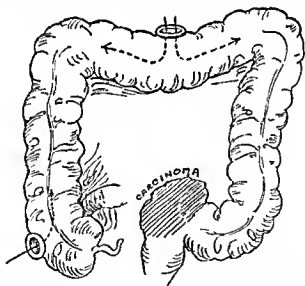


Fig 66—Carcinoma of sigmoid colon with obstruction preliminary colostomy. Cleansing preparatory to subsequent resection is more effective through a transverse colostomy than through a cecostomy

*Care of Preliminary Colostomy.*—When obstruction is not acute, the transverse colon may be exteriorized<sup>15</sup> and divided transversely after twenty-four hours by means of a cautery.

If distention becomes severe before this time, it may be relieved by aspiration of gas from the bowel by means of a hypodermic needle. After the colostomy has been opened, it is allowed to drain into bulky dressings, changed as necessary. When obstruction is acute and requires decompression without delay, cecostomy is performed as an emergency procedure, the distended cecum being opened at the time of operation and a rubber tube (one-fourth inch diameter) tied in with a double purse-string suture. The tube is connected to a drainage bottle at the patient's bedside on return to the room.

Irrigations with normal salt solution are begun five to six days following establishment of drainage and are performed twice daily, 1 liter of solution warmed to body temperature being used. Several hundred cubic centimeters of fluid are introduced at a time and are aspirated or drained out. A large amount of impacted feces will usually be recovered; the mass sometimes is so desiccated that it is necessary to introduce several ounces of warm cottonseed oil into the colostomy to soften the accumulation. Irrigations are discontinued as soon as complete evacuation of the retained feces has been accomplished. After the bowel has been washed clean, sulfasuxidine, 4.0 Gm., or sulfathalidine, 2.0 Gm., can be powdered, suspended in water, and introduced into the colostomy twice daily. If the colostomy is a tangential one, administration of the drug by mouth will establish satisfactory concentrations in the colon, although instillation of additional amounts directly into the bowel can do no harm and will probably be of benefit. If the colon is divided either halfway or completely across, however, no dependence can be placed upon oral administration of intestinal antiseptics; the drug must be introduced directly into the distal limb of the colostomy.

After twelve to fourteen days the obstructed bowel will have regained its normal nutritional state and operative resection can be undertaken safely. A final irrigation of the bowel is performed through the colostomy twenty-four hours before operation and an enema is given per rectum. Before the patient is sent to the operating room, an effort is made to drain out all retained fluid by means of a soft rubber tube passed from below and by thorough aspiration through a soft catheter introduced well into the distal loop of the colostomy.



If resection of the neoplasm is to be performed in one stage, an infusion should be begun while the patient is on the operating table and before the need for intravenous fluid has become apparent, so that a transfusion may be given through the infusion apparatus quickly and without loss of time if it becomes necessary.

Operations for the removal of a carcinoma of the colon are of two general types: primary one-stage resections with immediate anastomosis and obstructive resections performed in two or more stages. Postoperative care varies with the type of surgical procedure performed. In all cases, however, one liter of dextrose (5 per cent) solution is given intravenously when the patient is returned to the room, and a total of 3,000 c. c. of fluid should be given parenterally during the first twenty-four hours after operation. The condition of the patient should be watched closely and blood transfusions administered as soon as any evidence of impending shock is noted. Blood transfusion should be employed as a routine procedure before and after major operations upon the large bowel. Penicillin in full dosage may be given for five days after operation as a routine prophylactic measure.

**PRIMARY ANASTOMOSIS OF THE LARGE BOWEL.**—Primary anastomosis of the large bowel may include resection of a neoplasm with end-to-end or lateral anastomosis or the establishment of an ileocolostomy as the first step of a graded procedure for subsequent removal of the intervening colon. The suture line must be protected from tension to avoid the development of an intraperitoneal leak. Institution of suction drainage by means of a gastroduodenal tube or a Miller-Abbott tube introduced before operation and allowed to remain following operation will prevent distention of the bowel by retained fluid and swallowed air.

Nothing except liquids is given by mouth for four days after operation; nutritional and fluid balances are maintained chiefly by the administration of adequate fluids, salt, and dextrose by parenteral routes. Transfusions of blood are given and infusions of protein hydrolysate solutions are used to supply needed protein. Administration of vitamin concentrates should be continued. Morphine is used rather sparingly because

of its tendency to induce increased tonus in the small bowel and distention in the colon; peristaltic stimulants are strictly avoided. No enemas or cathartics are permitted. This very important order should be noted in red ink on the patient's chart and on the ward defecation sheet. Passage of a rectal tube is permissible only if the anastomosis is located above the level of the sigmoid. Sometimes the patient will be returned from the operating room with a soft rectal tube extending through and beyond a primary anastomosis in this region, which has been inserted from below under guidance of direct vision before closure of the abdomen (Stone<sup>16</sup>).

As in all gastrointestinal anastomoses, the period of danger extends from the third to the eighth postoperative day. If leakage of bowel contents occurs as the result of imperfect intestinal suturing or necrosis due to poor blood supply, it will usually appear during this period. If the leak is small and the vascularity is good, a transient and localized peritonitis of mild degree may develop, sometimes with the formation of a localized abscess. Gross leaks, rupture of a suture line, or necrosis following interference with the blood supply will quickly produce a generalized peritonitis and result in wide separation of the anastomosed bowel ends. Operation is of little use in either case; full doses of streptomycin and penicillin are given parenterally. A localized abscess may be drained later, after the bowel repair has healed and begun to function, but nothing will save the patient if the anastomosis has opened widely. Mechanical intestinal obstruction occasionally develops a week or more after operation, although this complication is less likely to occur if gastroduodenal suction drainage or drainage of the small intestine by means of a Miller-Abbott tube is established early in the postoperative course.

After the second day the patient may be given small amounts of water by mouth, and a diet of surgical liquids is permissible after the third day. After the fifth day a soft low-residue diet is prescribed and is continued for another week. The diet is increased to some extent after this time but should still be of the low-residue type for several weeks after recovery (Appendix). Protein hydrolysate preparations are given intravenously and orally after the second day and are continued until the patient is able to take a soft low-residue diet. At this time, intermediate

nourishments containing one or more ounces of skim-milk powder are added to the diet and are given at least three times daily throughout the period of convalescence.

**OBSTRUCTIVE RESECTION.** — Obstructive resection of a tumor-bearing area of the colon can be performed by one of the several accepted modifications of the Mikulicz procedure. The preoperative procedures required are similar in every respect to the measures instituted before primary resection and anastomosis. It must be noted again that while surgical decompression probably is an unnecessary preliminary in the absence of clinical colonic obstruction, the establishment of a functioning cecostomy or transverse colostomy is an absolute prerequisite to any form of operative removal of a colonic tumor which has caused alterations in nutrition of the proximal bowel wall as a result of obstruction or inflammation.

Following an obstructive resection the patient is returned from the operating room with the two ends of the bowel projecting through the abdominal wall, one and one-half inches above the level of the skin, each transected end closed by a clamp. Although the colon is totally obstructed as a consequence, complete occlusion in the absence of vascular damage is well tolerated for one or two days. The clamp on the proximal loop may be removed safely after forty-eight hours, but the clamp on the distal loop, which causes no clinically significant obstruction, may remain for three days or more. Occasionally, evidences of marked distention may develop rapidly in the proximal obstructed loop; the retained gas may then be evacuated simply by perforating the bowel just below the clamp with a hypodermic needle and releasing or aspirating the gas, or by relaxing the clamp on the proximal stump, gently inserting a soft 14 French catheter<sup>17</sup> deeply into the lumen, and replacing the clamp halfway across the bowel end to tighten the bowel around the tube and prevent leakage. Either of these procedures is preferable to the removal of the obstructing clamp before the abdominal cavity has become sealed off; leakage of infective material into the abdominal incision will result in wound infection, or, less frequently, in peritonitis. If a catheter is introduced into the proximal limb of the colostomy, it is not necessary to remove the clamp entirely for several days, when clamp and tube are removed together.

Before either obstructing clamp is removed, the surrounding abdominal wall and the region of the incision should be coated thickly with aluminum or kaolin paste or rubber cement, and some form of abdominal binder should be applied (Montgomery dressing) which will permit change of gauze without removal of adhesive tape fastenings. After the colostomy has been opened, the dressings may be changed by the nurse whenever necessary.

The exteriorized bowel must be inspected carefully during the first postoperative day for evidences of circulatory damage. If it becomes apparent that the blood supply of either end is impaired and that gangrene is impending, the sutures fixing the bowel to the skin should be removed and the bowel should be drawn farther out of the wound until a well-vascularized segment appears. This procedure is possible, however, only if the bowel was not fixed to the peritoneum at the time of operation. In such a case, the patient is returned to the operating room and the nonviable bowel is fully exteriorized by aseptic technique.

Difficulty may be encountered in combating intestinal distention following obstructive resection when the area of bowel removed includes the cecum and ascending colon, since the proximal clamp, in such a case, includes the open end of the terminal ileum. Such a temporary block of the small intestine is avoided when a primary anastomosis of terminal ileum and transverse colon is performed, but it is an annoying problem when a modified Mikulicz procedure is used. The obstructive symptoms can be prevented by the preoperative introduction of a Miller-Abbott tube or can be relieved, with less safety, by the early removal of the obstructing clamp. This complication may also be avoided by the Lahey method of "staggering" the bowel ends.<sup>18</sup> By this procedure an inch or more of devascularized ileum is allowed to project beyond the viable bowel after closure of the incision so that the obstructing clamp may be removed immediately and a rubber tube tied into the end of the ileum without contamination of the wound. Within several days the avascular segment sloughs off down to the level possessing a normal blood supply, which was fixed parallel to the end of the colonic segment at the time of operation and which then becomes the end of the ileostomy stump.

Intra-abdominal complications are not frequent, but they are serious when they do occur. If the bowel wall has been sutured to the peritoneum, the stitches may pull out as a result of postoperative straining or coughing, with consequent leakage and peritonitis. Insufficient mobilization of the bowel, with establishment of a colostomy under tension, may result in interference with the blood supply, retraction of the exteriorized segment into the wound or even into the abdomen, or intestinal obstruction as the result of kinking. Severe wound infection or even complete wound separation may result. Failure to close the rent in the mesentery following resection may permit the development of an internal hernia of the small intestine, with obstruction and rapid strangulation (Fig. 67). The possibility of postoperative mechanical intestinal obstruction is perhaps especially great in this group of patients and close watch should be maintained for evidences suggestive of this complication.

In other respects, general care following obstructive resection of a neoplasm of the colon is much the same as that after any intra-abdominal operation; the same untoward incidents may occur, and the same general prophylactic measures should be followed. Carbon dioxide inhalations are advisable during the first twenty-four hours, and the patient should be encouraged to move about in bed and to change position frequently.

Fluid and electrolyte needs are supplied by the administration of the proper amounts of normal salt and dextrose solutions parenterally, and blood transfusions are given as indicated. If a Wangenstein gastroduodenal suction tube has been introduced, the patient may be given tap water by mouth in small amounts. Otherwise, oral fluids are withheld until the proximal obstructing clamp has been removed. After the upper bowel loop has been opened, water in small quantities by mouth is permissible after cessation of postoperative nausea, and a surgical liquid diet may be given as soon as the patient desires it. The diet is increased as rapidly as desired.

Preparation for reanastomosis of the two loops of the spur is begun from ten to fourteen days after operation, by the introduction of a crushing clamp or enterotome into the bowel with one blade in each loop. When the clamp is closed, the septum between the bowel loops is crushed, and the resultant slough-

ing of the intervening wall converts the double-barreled colostomy into a single open channel. The Ochsner clamp or some modification thereof is satisfactory, although one of the spur-crushing devices individually adapted for the various types of spur colostomies is preferable. The enterotome usually drops off spontaneously in forty-eight to seventy-two hours, when separation of the crushed septum is complete. The instrument may have to be reapplied if too much of the intervening wall remains. Application of the crushing clamp to

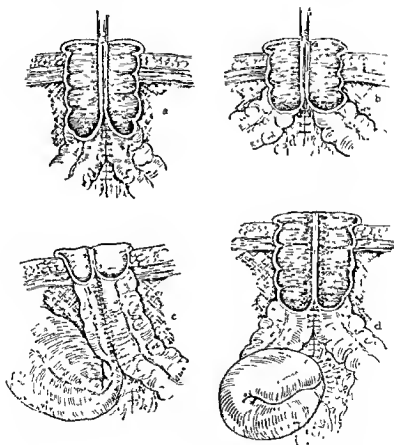


Fig 67.—Obstructive resection of the colon. *a*, Properly performed colostomy; crushing of spur. If the enterotome has a narrow blade two or three applications may be needed. *b*, Improperly performed spur colostomy. The spur is too short; application of the enterotome may be followed by peritonitis. *c*, Improperly performed colostomy; suture of the bowel under tension, with insufficient mobilization of the proximal loop and subsequent obstruction. *d*, Improperly performed colostomy; herniation and strangulation of small bowel through unsutured rent in mesentery.

the spur is inoderately unpleasant to the patient but not actually painful. If severe pain is produced or if nausea or vomiting develop, it is probable that either the mesentery or the free peritoneal surface of the colon has been caught in the clamp. Attempts at crushing the spur are abandoned under these circumstances and the colostomy is closed by reanastomosis of the two ends under direct vision.

After the intervening wall of the spur has been crushed adequately, the patient usually begins to pass feces per rectum, although the colostomy continues to function also. Within eight to twelve weeks, after the colostomy has spontaneously shrunk to a minimal size, it is customary to dissect the bowel cleanly away from the abdominal wall down to the level of the peritoneum and to close the stoma. This final stage is a relatively minor procedure, and no special measures need to be taken except to administer an intestinal antiseptic sulfonamide drug in the usual way, to clean the colon thoroughly before operation, and to institute a low-residue diet for several weeks afterward. Many surgeons have given up the method of colostomy closure by spur crushing and subsequent repair, preferring to take down the colostomy, dissect apart the two bowel loops, and perform an end-to-end anastomosis. This more accurate form of repair has gained in popularity since the introduction of intestinal antiseptic drugs and was practiced as a procedure of necessity in military service during World War II, in which colostomies were performed in the forward hospitals and closed in the larger installations farther to the rear. Since military records as to the type of colostomy and length of spur were not always complete, it was found to be safer therefore to prepare the bowel and close the divided colon by direct reanastomosis. This method appears to be less troublesome, less time consuming, and no less safe than the standard older procedure.

*Wound infection* is more common following operations upon the colon than after any other type of abdominal operation. It has occurred most frequently following graded procedures. If the incision is examined frequently, evidences of inflammation are often noted even before systemic signs of infection appear. Localized areas of induration must be opened and drained as soon as they develop, and the skin sutures are removed from the affected area. Local irrigations with Azochloramid in normal

salt solution (1:3,300) or with sodium sulfadiazine (0.5 per cent) or penicillin solution will prove of value in some cases, or the wound may simply be packed with fine-meshed gauze. Full therapeutic doses of penicillin are given parenterally, and administration of streptomycin may become necessary. Wound infection due to a subcutaneous leak in the proximal loop, to retraction of the colostomy into the wound, or to wide separation of the wound edges will sometimes necessitate the temporary establishment of another double-barreled defunctionalizing colostomy proximal to the infected area. When it appears that this step will be necessary or of sufficient benefit, there should be no delay in performing the operation, even though it does require further surgery and further hospitalization. Very little can be accomplished by local attack upon a retracted colostomy discharging into a widely opened, sloughing wound; the fecal current must be diverted before complete dehiscence of the wound and contamination of the peritoneal cavity occur.

**ABDOMINOPERINEAL RESECTION.**—Abdominoperineal resection, whether performed as a one- or a two-stage procedure, is an operation of considerable magnitude, and the patient should be brought into the best possible condition before operation by the methods already detailed. Enough time should be taken to establish a proper nutritional and fluid balance, to bring the hemoglobin content of the blood to a fully normal level, and to cleanse the colon thoroughly.

The general management of the patient following abdominoperineal resection of the rectum is much the same as that following any severe and potentially shocking operation. Blood transfusions are given routinely and full doses of penicillin are administered for several days after operation in all cases. Specific measures for care of the abdominal colonic stoma do not differ from those employed in the management of a double-barreled colostomy.

Peritonitis and intestinal obstruction due to adhesions are somewhat more likely to appear as complications after this procedure than after resection of carcinoma at higher levels in the colon.

*Urologic complications* are frequent following abdominoperineal resection of the rectum. Injury to a ureter or to the bladder during the course of the operation must be immediately



repaired if the accident is discovered. If a ureter has been divided or the urinary bladder has been opened unwittingly and is left unrepaired, there will be a constant leakage of urine from the perineal wound. The formation of a ureteral fistula usually necessitates subsequent nephrectomy, but a rent in the bladder can be repaired at once and should be drained for two weeks by means of a retention urethral catheter.

Urinary retention is a very common complication of abdominoperineal resection. There are several contributory causes, such as pre-existing urinary tract disease, slight cystocele in women, and slight prostatic hypertrophy in men, although the postoperative sagging of the bladder into the evacuated pelvis and the temporary injury to the parasympathetic vesical nerve supply<sup>19</sup> are sufficient in themselves to produce temporary urinary retention.

A retention catheter is introduced routinely before operation, a Pezzer catheter being preferred in women and a Bardex type of catheter in men. When a catheter is not used, overdistention of the bladder is likely to develop and the patient must be watched closely for inability to void and for overflow incontinence; repeated catheterization may be necessary. The retention catheter is connected to a drainage bottle at the bedside or to an apparatus that permits intermittent irrigation (Fig. 19). Normal bladder function usually returns within four to six days and the catheter may be withdrawn. A check for residual urine is made once or twice a day for two days; if the amount retained after voiding exceeds 30 c.c., the catheter is replaced for one or two days. Prophylactic administration of sulfadiazine or sulfacetimide is advisable in such cases to prevent the development of urinary tract infection.

Following complete resection of the rectum the *perineal wound* requires constant attention for the first few days after operation. The large dead space in the pelvis is lined in the operating room with a sheet of gutta percha or rubber dam and then packed with a long gauze roll to prevent immediate sagging of the pelvic floor, postoperative hemorrhage, and collection of serous fluid. Removal of the gauze pack is begun two days after operation and the gradual withdrawal occupies three to four days. At the end of this time the rubber pack also is withdrawn from the wound. If cigarette drains are used in preference to

the perineal pack, they may be withdrawn safely on the fourth or fifth postoperative day.

Postoperative hemorrhage is not often encountered. Excess exudation of fluid may be due to injury to the urinary tract, to a slight separation of the peritoneal closure, or to simple transudation of fluid from the traumatized surfaces. If hemorrhage does occur, and firm packing of the perineal wound does not stop the loss of blood immediately, the patient should be given a transfusion of blood and returned to the operating room for ligation of the bleeding vessel.

Infection of the perineal wound is largely preventable and depends to a great extent upon the degree of contamination at the time of operation and upon the quality of the postoperative management. Although the gauze packing should be snug, it should not be wedged in tightly enough to cause persistently uncomfortable and dangerous pressure, nor should it obstruct free drainage of exudate. If the drainage becomes purulent and malodorous several days after operation, the pack should be removed and one or two soft rubber catheters substituted. The cavity then may be irrigated gently under sterile precautions with a mildly antiseptic aqueous solution (such as Azochloramid, 1: 3,300, or potassium permanganate, 1: 5,000), with a saturated solution of sulfanilamide 0.8 per cent in normal salt solution, or simply with sterile normal salt solution alone, warmed to body temperature. Introduction of powdered sulfanilamide into the infected wound cavity is probably of little value. Penicillin or streptomycin, as indicated, is given systemically in full dosage. After the cavity has become partially obliterated by formation of granulation tissue and the patient has recovered sufficiently to be allowed out of bed, any remaining infection can be controlled readily by sitz baths once or twice daily in addition to irrigations of the wound, which are done routinely in all cases once or twice each day following removal of the pack.

*Perineal resection of the rectum of the Mummery type* combined with a double-barreled abdominal colostomy is managed locally in the same way. Following such an operation, however, there is some danger that the blind closed perineal stump of the distal loop of the colon may break open and discharge through the perineal wound. The distal loop is usually comparatively clean and the complication, although unfortunate, is not very

serious. Repair should not be attempted until after several months have passed in order to avoid entry of the peritoneal cavity from below in the early postoperative period. In most cases, moreover, closure of the fistula will occur spontaneously.

After the performance of the perineal operation, a small plug of petrolatum gauze may be inserted gently a short distance into the lumen of the distal colostomy loop and fastened to the abdominal wall by means of a securely attached thread. If the plug is permitted to remain until danger of postoperative breakdown of the perineal colonic stump is past, it will prevent contamination of the pelvic wound with feces in case the distal blind end of bowel does break open.

**Care of Permanent Colostomy.**—Care of a permanent colostomy is based upon the thorough education of the patient in the principles of dietary control. Most patients and many physicians are unaware that a colostomy can be managed so efficiently without the use of a bag that the ordinary social and business life of the individual will suffer little restriction. Completely satisfactory control of colonic evacuations can be developed in almost all cases, but will require a closely supervised training period of four to six months. If the patient can be convinced of this fact, much of his justifiable objection to a permanent colostomy will be overcome.

Education in care of the colostomy commences before discharge from the hospital. Irrigations are begun eight to ten days after operation and are performed regularly at two-day intervals thereafter. The patient is shown how to administer the enema slowly and collect the drainage in a basin pressed against the abdominal wall; he performs the task several times under supervision of a physician or nurse. He is cautioned to lubricate the tube thoroughly, to insert it gently, with a slight twisting motion, and never to try to force it past a temporary obstruction. If the tip of the tube catches in a mucosal fold during insertion, it can be freed by injection of a small amount of water. It is advisable also to indicate by a mark on the tube the proper distance for insertion to avoid possible damage to the bowel below the peritoneal level.

A low-residue constipating diet (p. 802) is prescribed and progressively amplified as regularity of colonic evacuation be-

comes established. Fluids are taken in small quantities and only at mealtimes for the first few weeks, after which their intake may be regulated by the patient. After evacuation control has developed, the diet may be almost normal in extent, although there are usually a few dishes, such as fried foods, baked beans, and corn, which are best omitted permanently from the diet.

Evacuation of the colonic stoma should be so regulated that discharge occurs only when irrigation is performed, at two-day intervals for the first two to three months and at three-day intervals thereafter. The enema is always given at a definite and regular time, preferably just before retiring; the simplest method of administration is by means of a standard enema bag equipped with a shut-off clamp and a catheter (22 French), a pint of water at a time being introduced slowly. The patient sits on a stool placed directly in front of the toilet; the evacuation can be collected in a pail or basin held against the abdomen or may be directed into the toilet by means of a commercial type of colostomy irrigator or a heavy rubber sheet rolled to form a trough.

Bowel movements in the intervals between irrigations are prevented by strict adherence to the constipating diet and by restriction of fluids. New foods can be added to the diet one at a time in small quantities, to determine their acceptability. If insufficient constipation or slight diarrhea should develop, occasional doses of paregoric or bismuth subcarbonate will quiet the overactive peristalsis. No cathartics, not even mineral oil, should ever be used; emptying of the colon must be accomplished only by irrigation. In occasional cases, careful observance of dietary restrictions and of regular irrigation eventually may bring about habitual spontaneous and unaided peristaltic evacuation of the bowel at a regular time each day or two.

Less than one-third of all colostomy patients require a bag or pouch, and, since this apparatus encourages prolapse of the proximal loop, it should not be employed unless absolutely necessary. A simple web or elastic belt six inches wide for male patients or a girdle for female patients will serve to hold a small dressing snugly against the stoma; the dressing will need to be changed only two or three times a day.

### Anus

**Proctoscopic examination** is usually performed as a preliminary to surgical procedures upon the anus, since symptoms apparently referable to diseases of the anal region are often due to the presence of a more extensive or more serious lesion at a higher level. Three-fourths of all rectal carcinomas are within reach of the examining finger, and two-thirds of all carcinomas of the large bowel are within reach of the sigmoidoscope. Most neoplasms of the left side of the colon therefore can be diagnosed during the early clinical stages. Any history of recent noticeable alteration in bowel function or of rectal bleeding indicates the necessity for digital and proctoscopic examination, even if the presenting symptoms can be explained entirely adequately by an obvious rectal or anal lesion.

Little local preparation is necessary before a sigmoidoscopic examination except the administration of two enemas, one to be given the night preceding examination and the second four hours before. All the fluid used in the enema must be drained out before the sigmoidoscope is introduced. If the suspected lesion is inflammatory in nature (*ulcerative colitis, amebic dysentery, bacillary dysentery*), the preparatory enema is omitted because it alters the appearance of the rectal mucosa for a short time. No anesthesia is required, although the patient may tolerate the instrumentation better if morphine, 8 to 10 mg. (gr. 1/8 to 1/6), is administered hypodermically fifteen minutes before examination. As a general rule, the knee-chest position offers satisfactory and convenient exposure and allows the sigmoid colon to straighten out by gravity. A special effort should be made to secure the patient's complete cooperation in order to secure proper position. A pillow is placed beneath the subject's chest, the head is turned to one side, and the elbows are allowed to drop over the edge of the examining table. The toes project over the lower edge of the table, the line of the thighs is directly vertical, and the knees are slightly separated. Finally, the patient is instructed to let his back sag down. It is important to note that the weight of the subject's trunk should rest on his chest; he must not be permitted to lean on the elbows or to arch the back. The presence of diarrhea ordinarily prevents proctoscopic examination, although the procedure may be performed with reasonable safety if the patient is placed prone on

the table in a fully inverted position; that is, the head rests on the headpiece of the table, the trunk and pelvis are perpendicular to the floor, the thighs and knees are flat on the table, and the legs extend straight up. The proctoscope is then introduced directly downward (Fig. 68). The obturator is withdrawn as soon as the end of the tube passes beyond the sphincter, further introduction is made under direct vision.

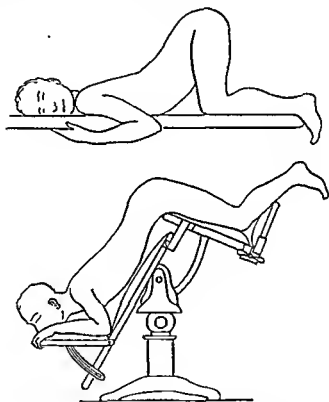


Fig 68 —Positions for proctoscopic examination. Upper figure shows knee-chest position. Lower, inverted position.

Preparation for the simpler operative procedures for non-inflammatory lesions of the anus is more or less uniform. The patient is admitted the day before the proposed operation, and the usual complete general physical examination, blood count, and urinalysis are performed. A light supper is permitted, and nothing but water is allowed by mouth after midnight. An enema is given before the patient retires, with sedatives or

hypnotics as needed. Another enema is administered the following morning three hours before the time for operation, and the patient is given whatever preliminary medication is indicated. No cathartics are used, in order to avoid the possible passage of fluid feces during operation. The use of intestinal antiseptics before hemorrhoidectomy or fistulectomy offers no advantages and is not recommended.

**Hemorrhoids.**—Following hemorrhoidectomy, typical orders include surgical liquid diet; morphine, 10 to 16 mg. (gr.  $1/6$  to  $1/4$ ) hypodermically, if necessary, to be repeated if necessary; horizontal position for twenty-four hours, especially following spinal anesthesia; and mineral oil, 15 to 30 c.c. (oz.  $1/2$  to 1), each night and morning to prevent the formation of a constipated stool.

A rectal plug employed to prevent postoperative bleeding is removed within twelve to twenty-four hours. Rectal plugs usually consist of a twisted strip of petrolatum gauze or of a folded piece of lubricated rubber dam with a small tube through the center to permit the escape of flatus. If the plug interferes with evacuation of the bladder or causes too much pain, it may be removed at any time.

On the second morning after operation the patient is given  $1/2$  ounce of magnesium sulfate or Rochelle salt, and regular diet is permitted after the first bowel movement. Sitz baths once or twice daily may be instituted at this time. On the fifth day, a well-lubricated gloved finger should be inserted gently into the anal canal past the sphincter to prevent development of constricting adhesions and scar tissue. This procedure is to be repeated every two days until healing has occurred, although the patient is usually able to leave the hospital after the sixth postoperative day. The use of mineral oil is continued until after the operative wound has completely healed.

According to personal preference, another measure which may be instituted during the period immediately following hemorrhoidectomy is the use of hot wet normal saline dressings, to be changed hourly. Although compresses are usually unnecessary, their use may add to the patient's comfort following an extensive hemorrhoidectomy. The only laxatives permitted are saline cathartics, which produce a thin fluid stool, and mineral oil, which acts simply as a lubricant. Some authorities object

even to these medications and prefer to avoid postoperative constipation by permitting a soft or regular diet the day after operation and administering 6 ounces of cottonseed oil as an enema on the third night after operation, to be retained overnight and flushed out with a small enema of normal salt solution the following morning. Whatever postoperative routine is followed, some steps must be taken to prevent the development of constipation, and the patient must be encouraged to move about in bed actively.

Upon discharge the patient is advised to take daily sitz baths at home until healing of the operative wound is complete. Advice should be given concerning proper habits of food and fluid intake, avoidance of the use of cathartics, and establishment of a regular routine time each day for evacuation of the bowels. The use of mineral oil may be continued as long as necessary.

The two most important complications of hemorrhoidectomy are persistent hemorrhage and intractable pain. Bleeding is common after surgical procedures upon the anus and may continue for an unduly long time if the blood is allowed to accumulate in the rectum. Digital evacuation of the clotted material may stop the bleeding; otherwise, a dry fine-meshed gauze pack should be inserted. Pressure on the bleeding point may be secured with a minimum of pain to the patient if a strip of gauze 8 or more inches in length is threaded with a suture, introduced well above the sphincter, and then pulled down snugly against the region of the sphincter by the ends of the thread (Fig. 69). A pack of oxidized cellulose (absorbable) gauze also will stop such bleeding; only a small amount should be used, since it promptly breaks down into a sticky gelatinous mass which may interfere with evacuation of gas. Following every hemorrhoidectomy, a blood hemoglobin determination should be a routine procedure when the patient is discharged, and treatment for secondary anemia should be instituted when indicated.

Posthemorrhoidectomy pain is a usual feature of the convalescent period and cannot be entirely avoided. In most cases, repeated application of Nupercaine (1 per cent), Eucupin (1 per cent), or nutgall and opium ointment will be sufficient to afford the patient a reasonable degree of relief. Some surgeons, although admitting the inadvisability of performing subcutane-



ous injections in a contaminated field, attempt to prevent the development of posthemorrhoidectomy pain and sphincter spasm by the injection of an oil-soluble anesthetic at the time of operation. While the resulting anesthesia is not complete, the degree of pain during convalescence is considered to be greatly diminished by the procedure. The method is not yet accepted generally.

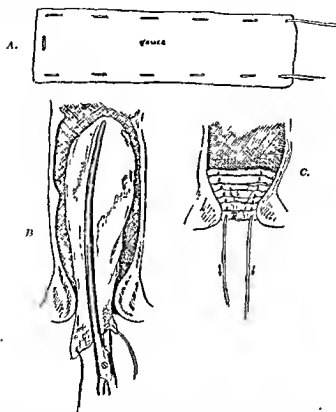


Fig 69.—Control of posthemorrhoidectomy bleeding. An opened fine-meshed gauze sponge is threaded, *A*, on three sides. The entire sponge is inserted into the rectum beyond the sphincter, *B*, and pulled snugly down against the bleeding point by traction on the threads *C*, which are then taped to the buttocks.

The most widely used nontoxic oil-soluble anesthetics include Proctocaine, Benacol, Anucaine, and Eucupin in oil, all of which are obtainable in ampules. A total of 8 to 10 c.c. is ordinarily sufficient. The left index finger is introduced into the rectum, both to avoid puncturing the rectal wall and to serve

as a guide for the point of the needle, and the solution is introduced through a long needle and syringe by the following method<sup>20</sup>: Two punctures are made in the midline, about 1 cm. above and below the anal margin. A small amount of the solution is injected in the region of the external sphincter from the posterior (lower) aspect, after which the needle is carried deeper, and infiltration is continued around the internal sphincter and to each side of the rectum, the entire posterior region thus being infiltrated in a wide, fanlike manner. The remainder of the solution is then introduced through the anterior (upper) puncture in the same way (Figs. 70 and 71).

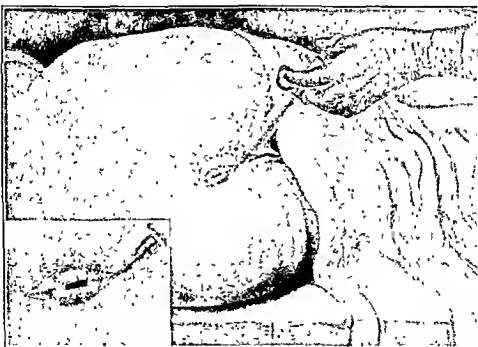


Fig. 70.—Injection of oil-soluble anesthetic for posthemorrhoidectomy pain illustrating the site of needle puncture (From Ault *Surgery* 6:757, 1939.)

Certain precautions are necessary when this method is employed. Only a small amount of solution should be injected in any one spot to avoid the development of necrotic areas, abscesses, and sloughs. For the same reason the direction of the needle should be changed very frequently and no oil should be injected just beneath the skin. A detailed account of the procedure can be found in the report by Morgan.<sup>21</sup>

The patient should be warned that *partial anesthesia* will persist for from one to two weeks following introduction of an oil-soluble anesthetic and that the *appearance of a slight urge to defecate* during this period indicates the necessity for immediate evacuation of the bowel.



Fig. 71—Injection of oil soluble anesthetic for posthemorrhoidectomy pain. Illustrating the superficial and deep planes of injection. The subcutaneous area with the vertical shading shows the plane of injection obtained by inserting the needle along the lines marked 1. The deeper injections are given along the lines marked 2, 3, 4, and 5. (From Ault, *Surgery* 5:759, 1939.)

**Fissure of Anus.**—Postoperative care following excision of an anal fissure is minimal. A narcotic may be required during

the first two days, and the stools should be kept soft by the regular oral use of mineral oil and an occasional dose of a saline cathartic. These patients also should be given careful instructions with respect to proper dietary and elimination hygiene.

Anorectal fistulas require considerable attention following operation to insure proper healing and to prevent recurrence. The surgical treatment of these fistulous communications between the rectum and the skin surface consists of the wide incision of the main tract in its entirety, including both openings and all secondary extensions. The success of the procedure depends upon the identification and wide incision of the internal opening, the removal of all redundant edges so that the entire fistulous tract is laid open, and the prevention of bridging of the wound by granulation tissue during the early postoperative period.

Care following an operation of this type is similar to that following hemorrhoidectomy. The gauze pack inserted at the time of operation is removed after forty-eight hours and the wound is inspected and examined digitally each day to make sure that granulations are developing from the base of the wound and that the edges are not healing together before the cavity is filled in. Sitz baths may be given once or twice daily after the third day, and a regular diet is permitted after this time.

It is sometimes necessary to divide the external anal sphincter during operation for a fistula with a high internal opening. As a consequence, sphincter control may be affected to a variable degree for some days or weeks after operation, and a constipating diet (Appendix, Colostomy Diet) should be adopted until normal function returns. Although division of the external sphincter is not necessarily followed even temporarily by total incontinence, the patient should be warned that control is impaired and that the appearance of even the slightest sensation of fullness in the rectum calls for instant evacuation. The effect of a constipating diet may be reinforced by the use of paregoric.

The wound should be inspected at least twice a week after the patient leaves the hospital until healing is complete. Surgical treatment of an extensive fistula with ramifying channels may require operation in two or more stages. A sufficient number of months must be allowed to elapse between each stage to insure the development of a strong and contracted scar so that wide

gaping of the sphincter may be avoided if it is necessary to divide this muscle at a subsequent stage

**Pruritus Ani.**—In patients afflicted with pruritus ani, the perianal skin is usually soggy, edematous, infiltrated, and cracked. Much of the edema and some of the itching may be relieved by the preoperative use of warm glycerine compresses. Other nonsurgical measures which provide at least temporary benefit in some cases include the use of x-ray therapy, the local application of preparations such as Calmitol, and the oral administration of antihistamine drugs, such as Pyribenzamine or Benadryl.

The condition is usually treated by the perianal subcutaneous injection of alcohol for the destruction of the cutaneous nerves of the perianal region. This procedure was originally described by Stone,<sup>20</sup> who advocates the introduction of 5 to 10 c.c. of 95 per cent alcohol by multiple punctures with a fine hypodermic needle. According to this technique, not over 0.2 c.c. is deposited at any one spot, and injections are made approximately 0.5 cm. below the surface of the skin and about 0.5 cm. apart, particular attention being paid to the region of the anterior and posterior commissures. By this method, complete relief is secured and the danger of subsequent sloughing is minimal. The modification preferred by Buie<sup>21</sup> consists of the use of 20 to 50 c.c. of 40 per cent alcohol to be introduced widely throughout the subcutaneous tissues of the perianal region. Infiltration is carried out through a single puncture wound on each side of the anus, with care to avoid deposition of too much alcohol at any one point. This technique, although it does achieve permanent relief of the pruritus ani, is followed in a high percentage of cases by extensive sloughing of the perianal tissues, with prolonged drainage of foul necrotic material. In order to obtain a cure of the pruritus by this method, however, so much alcohol must be introduced that perianal sloughing can be expected. Recurrence of pruritus is more common following alcohol injection by multiple puncture but can be treated successfully by reinjection.

Abscesses following the subcutaneous injection of alcohol are treated by hot wet dressings of normal salt solution changed hourly until the areas soften enough to permit incision. Open sloughs are treated by the use of hot compresses, with sitz baths several times daily. After the acute stage has passed, nitrofur-

zone solution or Azochloramid (1: 500 in triacetin) may be applied as often as necessary. Persistent infections in these areas sometimes respond to the use of zinc peroxide compresses.

Acute infections of the deep perianal, perirectal, or ischio-rectal tissues are surgical emergencies and demand immediate operation. Although the institution of surgical drainage through a perineal incision and insertion of a pack are simple procedures which require only a few moments, general anesthesia is necessary. A physical examination of the heart and lungs therefore is indicated, and a blood pressure determination and urinalysis also must be made before induction of anesthesia. No further preparation is required. Even the slightest trauma to the inflamed rectal mucosa must be avoided in order to prevent subsequent formation of a fistula.

Postoperative care is similar to that following a hemorrhoidectomy, although some surgeons may prefer to keep the patient constipated for several days. Colonic peristalsis can be depressed, if desired, by administration of paregoric for as long a period as necessary. Other orders are the same as for hemorrhoidectomy with omission of the use of mineral oil. When evacuation of the bowel is finally desired, a saline cathartic may be given. The gauze pack, used in all cases, may be removed one or two days after operation.

Plastic operations upon the anus, such as the Wreden-Stone procedure for relief of incontinence, require thorough cleansing of the bowel for seven to ten days before operation by the use of a low residue diet and daily enemas. Rochelle salt or magnesium sulfate, 15 Gm. (oz. 1/2), is given on the morning following admission and sulfathalidine is administered in full dosage for from seven to ten days.

Since the success of the procedure depends largely upon the avoidance of postoperative wound infection, complete constipation is necessary for the first few days of the convalescent period. Sulfathalidine is continued, and a small dose of paregoric is given twice daily, beginning the day before operation or on the operative day and continuing for several days after. No cathartics, not even mineral oil, should be administered until ten to fourteen days after operation. The patient is given a surgical

liquid diet for several days after operation and then a low-residue soft diet until healing is assured. Intravenous fluids are given as indicated. The patient lies on the abdomen with no covering over the buttocks and no dressing upon the wound. A cradle is used to support the bedclothes, and the operative area is kept clean by the attending nurse.

Competent care before and after rectal plastic operations is a factor of the greatest importance in assuring a satisfactory outcome. In order to avoid the possibility of a thoughtless mistake, it may be wise to note in red ink on the patient's chart and on the ward defecation sheet that no medication or treatment by rectum is permissible, not even the passage of a rectal tube, and that cathartics are forbidden.

Care before and after operations for repair of a divided anal sphincter, as in a third degree perineal laceration, is much the same, except that the patient is permitted to move about in bed as desired.

### References

1. Stone, H. B.: Surgical Problems in the Treatment of Chronic Ulcerative Colitis, *Arch. Surg.* 41: 525, 1940.
2. Streicher, M. H.: Phthalylsulfathiazole, *J. A. M. A.* 129: 1080, 1945.
3. Dennis, C.: Ileostomy and Colectomy in Ulcerative Colitis, *Surgery* 18: 435, 1945.
4. Stone, C. A., and Roddenbery, S. A.: A Modification of the Gius-Racely Portable Suction Apparatus, *Surgery* 18: 598, 1945.
5. Lium, R.: Suction Tube for Ileostomy, *New England J. Med.* 216: 345, 1937.
6. Lahey, F. H.: Discussion of the Modified Mikulicz Operation for Carcinoma of the Colon and Its Technic, *S. Clin. North America* 26: 611, 1946.
7. Stone, H. B., and McLanahan, S.: Resection and Immediate Aseptic Anastomosis for Carcinoma of the Colon, *J. A. M. A.* 120: 1362, 1942.
8. Rankin, F. W.: The Principles of Surgery of the Colon, *Surg., Gynec. & Obst.* 72: 332, 1941.
9. Wangenstein, O. H.: Primary Resection (Closed Anastomosis) of the Colon and Rectosigmoid, *Surgery* 11: 403, 1943.
10. McNealy, R. W., and Lands, V. G.: Primary Anastomosis in the Treatment of Carcinoma of the Colon, *Surgery* 21: 283, 1947.
11. Meyer, K. A., Sheridan, A., and Kozoll, D. A.: One Stage "Open" Resection of Lesions of the Left Colon Without Complementary Colostomy, *Surg., Gynec. & Obst.* 81: 507, 1945.
12. Poth, E. J.: Succinylsulfathiazole and Phthalylsulfathiazole in Surgery of Colon, *Surgery* 17: 773, 1945.

13. Whipple, A. O.: Surgery of the Terminal Ileum, Cecum, and Right Colon, *Surgery* 14: 321, 1943.
14. Allen, A. W., Welch, C. E., and Donaldson, G. A.: Carcinoma of the Colon, *Ann. Surg.* 126: 19, 1947.
15. Fallis, L. S.: Transverse Colostomy, *Surgery* 20: 249, 1946.
16. Stone, H. B.: Discussion of Rankin, F. W.: Value of Cecostomy as Complementary and Decompressive Operation, *Ann. Surg.* 110: 380, 1939.
17. Boehme, E. J., and Cattell, R. B.: Cancer of the Rectum. A Discussion of Preoperative Preparation, Postoperative Complications, and Colostomy Management, *S. Clin. North America* 26: 564, 1946.
18. Lahey, F. H.: Resection of the Right Colon and Anastomosis of Ileum to the Transverse Colon After the Mikulicz Plan, *Surg., Gynec. & Obst.* 54: 923, 1932.
19. Kickham, C. J. E., and Bruce, N. H.: Urological Complications in Malignant Disease of the Rectum, *J. Urol.* 41: 541, 1939.
20. Ault, G. W.: Elimination of Pain Following Hemorrhoidectomy, *Surgery* 5: 755, 1939.
21. Morgan, C. N.: Oil-Soluble Anesthetics in Rectal Surgery, *Brit. M. J.* 2: 928, 1935.
22. Stone, H. B.: Pruritus Ani; Treatment by Alcohol Injection, *Surg., Gynec. & Obst.* 42: 565, 1926.
23. Buie, L. A.: Proctoscopic Examination and the Treatment of Hemorrhoids and Pruritus (Mayo Clinic Monograph), Philadelphia, 1931, W. B. Saunders Co.



## CHAPTER 21

### BILIARY TRACT

#### Preoperative Care

Surgical procedures upon the extrahepatic biliary tract may carry a high morbidity rate not only because of technical difficulties, but also because of the visceral damage produced by chronic infection and long-standing partial obstruction of the bile ducts. The presence of stones or of low-grade infection in the biliary tract is always associated with some degree of chronic diffuse intrahepatic cholangitis, with degenerative changes in the liver cells. Concomitant disturbances of function, moreover, are often found in other parenchymatous organs as well. Before operation can be undertaken safely, such patients require thorough and careful physical examination in order to detect any signs of visceral damage and to plan the necessary preoperative preparatory measures.

Cardiovascular disease is a frequent coincidental finding, and particular search must be made for an early history or for early physical signs suggestive of beginning heart failure or coronary disease. If the evidences of impaired cardiac function are equivocal, the degree of exercise tolerance should be investigated and an electrocardiogram and teleroentgenogram secured. Determination of the vital capacity also is indicated in the presence of cardiac or pulmonary disease, since surgical operations, particularly upon the upper abdomen, may decrease the vital capacity temporarily to one-third or one-fourth of its normal value. Patients with the milder forms of cardiac disease usually respond well to the institution of complete bed rest for a few days and an occasional dose of a sedative drug for restlessness. The use of digitalis is not advisable under any circumstances unless definite evidences of myocardial failure or auricular fibrillation are present.

Kidney function must be investigated in each case. Renal damage is often associated with hepatic disease, and low reserve kidneys may fail without warning following an operation upon the biliary tract.

A complete urinalysis, including examinations for bile and urobilinogen, a Fishberg concentration test, and a phenolsulfonphthalein excretion curve are simple procedures to perform and supply indispensable information. Elevation of the nonprotein or urea nitrogen of the blood is always significant of urinary retention. In an extremely ill patient, however, the liver function may be so greatly depressed that the formation of urea occurs at a subnormal rate. The nonprotein nitrogen and urea content of the blood may sometimes be relatively low for that reason, even in the presence of renal deficiency and oliguria.

**Liver Function.**—Although some degree of liver damage always results from disease of the extrahepatic biliary tract, the depression in hepatic function cannot easily be demonstrated by clinical tests. The hepatic reserve is of so great a magnitude that normal metabolic processes may be maintained even if 75 to 80 per cent of the liver substance is removed experimentally, and the rate of regeneration of the liver is so rapid that restoration of a damaged or excised area is accomplished within a few weeks. The same situation holds clinically; hepatic injury must be extensive before impairment of function becomes clinically evident or demonstrable. Measurement of the hepatic reserve or degree of damage as a whole is also impossible because of the wide variety of functions attributed to the liver. The laboratory examinations used at present for the clinical estimation of liver reserve test only single functions of the organ. Most tests, moreover, do not reveal any evidence of abnormality until a relatively severe degree of liver damage has occurred.

Some of the more important *functions* of the liver include the following:

1. The metabolism, storage, and release of carbohydrates; synthesis of glucose from amino acids, from other sugars (fructose, galactose), and from lactic acid produced in the muscles
2. The intermediary metabolism of proteins, including deamination of amino acids to form glucose or fat and urea, synthesis of nonessential amino acids, and partial destruction of uric acid.
3. The intermediary metabolism of fats, including oxidation to form keto-acids, which are utilized for energy in the tissues.
4. Formation of bilirubin from overaged and damaged erythrocytes by the reticulo-endothelial (Kupffer) cells. These

cells also phagocytize foreign material from the blood stream (particulate matter, bacteria).

5. Excretion of bile, containing bilirubin and bile salts, through the hepatic cells into the bile ducts.

6. Detoxication of various poisons (indole, skatole, phenol, benzoic acid).

7. Synthesis of prothrombin, under influence of vitamin K.

8. Formation of plasma proteins (fibrinogen, albumin, probably part of the globulins).

9. Synthesis of heparin, which is formed chiefly in the liver, although it is formed also in other tissues.

10. Formation of vitamin A from the provitamin (p. 207).

11. Storage of the antianemic factor, deficiency of which results in pernicious (primary) anemia. An extrinsic factor in the food is acted upon by an intrinsic factor (a gastric enzyme) to form the antianemic principle, which is stored in the liver.

12. Participation in regulation of body heat, both by metabolic activity and by altering the circulating blood volume.

13. Storage of iron and copper. The effects of this function are particularly noticeable in hemochromatosis, a disturbance of iron excretion in which large deposits of hemosiderin are found in the liver cells.

Bile is an alkaline fluid, containing bile salts, bile pigments, cholesterol, and lecithin, secreted by the hepatic cells into the bile capillaries and poured into the descending portion of the duodenum through the ampulla of Vater in quantities normally approximating 500 c.c. daily. The chief bile salts are sodium glycocholate and sodium taurocholate, formed by combination of glycine and taurine with cholic acid and with sodium. These salts are necessary for the activation of pancreatic lipase in the intestine and for the emulsification of fats and the absorption of fatty acids during digestion. The bile salts are reabsorbed from the intestine and are again excreted into the bile, continuing to pass through the same cycle. The chief bile pigment is bilirubin, formed by hydrolysis of hematin in the normal breakdown of old erythrocytes within the cells of the reticulo-endothelial system. Bilirubin is excreted through the hepatic parenchymal cells into the bile and is discharged into the bowel, where it is reduced to urobilinogen. Part of the urobilinogen is oxidized to urobilin in the stool, and part is reabsorbed into the blood stream and

again passes through the liver and, in small quantities, through the kidneys. Concentration of the bile takes place in the gall bladder. The solubility of cholesterol in bile depends partly upon the concentration of bile salts; if the cholesterol is increased or the bile salts diminished, a tendency to precipitation of cholesterol results. Formation of cholesterol gallstones is thereby encouraged.

Jaundice appears clinically as the result of an increase in serum bilirubin and may be of two broadly different types, obstructive and nonobstructive. The type of jaundice ordinarily seen by the surgeon is obstructive, caused by a block in the extra-hepatic biliary tract due to stone, neoplasm, or stricture. Non-obstructive jaundice may be toxic or infectious in nature, with a variable degree of parenchymal hepatic necrosis, or it may be hemolytic, with production of bilirubin from destroyed erythrocytes in quantities temporarily exceeding the capacity of the liver to excrete. Preparation of the patient for operative procedures upon the biliary tract is no longer emergency in nature. Even if severe and progressive jaundice is present, several days may be spent profitably in correcting the physiologic damage and increasing the liver reserve. The functional capacity of the organic systems should be estimated, the nature and degree of jaundice determined, and a diagnosis of the type and extent of the biliary and hepatic disease attempted. The most widely adopted tests of liver function<sup>1</sup> include the following:

#### TESTS TO DETERMINE THE NATURE AND DEGREE OF JAUNDICE.—

1. *Urinary examination* in obstructive jaundice reveals the presence of bile but no urobilinogen, even the normal small quantity being absent. In hemolytic jaundice the urine contains no bile but contains an increased amount of urobilinogen. The stool is light yellow or clay colored in obstructive jaundice because of the absence of bile but may be even darker than normal in hemolytic jaundice, in which unusually large quantities of bile are excreted.

2. The *icteric index* is a colorimetric comparison of clear centrifuged blood serum with standard solutions of potassium dichromate. Normal serum has a range of 4 to 6 icteric index units and subclinical jaundice a range of 6 to 15 units. If the serum

icteric index is above 15 units, jaundice is usually visible. Five cubic centimeters of oxalated blood should be secured for the test. A fasting specimen is preferable, since lipemia after meals may be sufficiently marked to cloud the serum.

3. The *van den Bergh test* for jaundice is based upon the facts that free bilirubin in aqueous solution, as in serum, will react with Ehrlich's diazo reagent to form a red dye and that combined bilirubin will diazotize in the presence of alcohol but not in simple aqueous solution. The reaction is immediate and direct in the presence of obstructive jaundice and indirect in jaundice of the hemolytic or retention types. Extrahepatic obstruction due to a malignant tumor is almost always complete and progressive, while block due to a calculus is transient and usually less than complete.

A generally accepted theory explaining the different *van den Bergh* reactions states that bilirubin, before passage through the liver cells, is carried in the blood stream in loose combination with protein and in this form is insoluble in water. In this form it will not be excreted into the urine and will give an indirect *van den Bergh* reaction. With entrance into the hepatic cells and excretion into the biliary ducts, however, bilirubin is separated from its protein combination and then, if reabsorbed into the blood stream, will pass through the kidneys into the urine and will give a direct *van den Bergh* reaction. Less dependence is placed upon the *van den Bergh* test than formerly as a method of differentiating obstructive from toxic jaundice, since free bilirubin, which gives a prompt direct reaction, is present in both of these types of jaundice when the level of serum bilirubin is high.

Five cubic centimeters of oxalated blood are secured for the test. One cubic centimeter of clear serum is placed in a tube, and 0.5 c.c. of freshly prepared Ehrlich's diazo reagent is added very slowly to form a distinct layer above the serum. A positive reaction, characterized by the development of a red ring between the layers, will usually appear within a minute but may be delayed as long as ten minutes. The delayed reaction is characteristic of jaundice due to liver damage.

For performance of the indirect test, 2 c.c. of 95 per cent alcohol is mixed with the serum. Upon addition of the reagent, a reddish-violet color develops immediately.

4. The *serum bilirubin test* is a quantitative determination. Normal serum contains from 0.3 to 1.0 mg. of bilirubin per 100 cubic centimeters. This test is more accurate than the icteric index determination but does not add much to the information supplied by the simpler procedure. It is carried out as a continuation of the indirect van den Bergh test.

5. *Serum alkaline phosphatase*, normally produced in bone, is excreted by the liver into the bile. Obstruction to biliary excretion therefore results in interference with alkaline phosphatase excretion, and the serum phosphatase level rises. Some elevation of this constituent may occur also in the presence of severe hepatic damage or neoplastic disease of the liver, or in association with certain diseases of bone.

#### TO DETERMINE THE DEGREE OF LIVER DAMAGE.—

1. The *rose bengal excretion test* is a colorimetric determination of the amount of the dye present in the blood three and nine minutes, respectively, after intravenous injection of 10 c.c. of a sterile 1 per cent solution of the dye. This test measures only the excretory function of the liver and detects only a marked degree of liver damage. The results are not always accurate and dependable; values approaching normal may be obtained even when the liver is moderately damaged.

2. The *bromsulfalein excretion test* is a colorimetric estimation of the amount of dye remaining in the blood five and thirty minutes, respectively, after intravenous injection of a 5 per cent solution of bromsulfalein in amounts totaling 2 mg. per kilogram of body weight. Normally only 25 to 40 per cent of the dye is present after five minutes and none is present after thirty minutes. This test is one of the most widely used dye excretion determinations for liver function in the absence of jaundice.

Macdonald<sup>2</sup> has stated that the dependability of the test is increased greatly if a curve of the rate of excretion of the dye is plotted, since a delayed curve will demonstrate liver damage even though the total quantity excreted within the usual thirty-minute period is normal. The procedure suggested is as follows: Venipuncture is performed with an intravenous needle attached to a collecting syringe fitted with a three-way stopcock, and a 5 c.c. sample of blood is withdrawn. The needle is allowed to remain in situ throughout the test, and normal salt solution is in-

troduced slowly to keep it open. Five milligrams of bromsulfalein per kilogram of body weight are injected slowly into another vein, and samples of blood are withdrawn at exact five-minute intervals by means of the collecting needle, a different syringe being used each time. Seven samples of blood are thus collected at equal intervals over the thirty-minute period. Macdonald believes that normally the dye is excreted completely within eighteen minutes and that a delayed excretion curve indicates the presence of liver damage, even though the thirty-minute total is normal.

3. The *galactose tolerance test* is a measure of the ability of the liver to utilize galactose, the quantity utilized depending upon the degree of hepatic efficiency. This sugar is slowly converted into glycogen by the normal liver and the excess is excreted quantitatively by the kidneys. The test, which is carried out in the morning on a fasting stomach, is performed by administering 40 Gm. of galactose in 50 c.c. of water flavored with lemon juice. Nothing else is given by mouth except water, which is permitted in any quantities desired. Specimens of urine are collected in separate containers each hour for five hours and are tested qualitatively for sugar with Benedict's solution. The specimens containing sugar are mixed together and the total quantity of contained carbohydrate is determined. Normally, not over 3 Gm. is lost in the urine; the excretion of more than 5 Gm. is definitely significant of advanced liver damage. The galactose tolerance test obviously cannot be used in the presence of glycosuria from diabetes or following dextrose infusions or in the presence of depressed renal function.

All three of these excretion tests are more or less unreliable, since significant changes do not appear until hepatic damage is marked. While positive results are of significance, negative results afford no information of dependable value.

4. The *tetraiodophenolphthalein retention test* was introduced by Graham as a method of cholecystography and later used also for estimation of liver function. For visualization of the gall bladder, the dye is ordinarily given by mouth, under which circumstances it cannot be used as a test of liver function. Normal retention of the dye thirty minutes after intravenous injection averages 10 to 15 per cent; retention of 50 per cent or over indicates the necessity for careful preoperative preparation. This

test should not be used in the presence of jaundice or of severe systemic disease.

5. The *Quick hippuric acid test*<sup>2</sup> is a widely used and dependable test of liver function. Benzoic acid, which is administered in a measured dose, is quantitatively conjugated in the liver with aminoacetic acid to form hippuric acid, which is eliminated in the urine. Since aminoacetic acid is synthesized by the liver at a maximum hourly rate which cannot be exceeded no matter how much benzoic acid is administered, the proportion of a test dose of benzoic acid excreted in the urine as hippuric acid within a definite time limit is a rough index of the degree of liver function, at least in regard to detoxication. Positive evidence of minor degrees of hepatic injury can be detected by this test in most cases and, since the test is a harmless one, the improvement of liver function in response to proper therapy can be gauged by repeated tests. A single test, in fact, is inconclusive; the test should be repeated on several occasions to obtain dependable information. The obvious shortcomings of the Quick test are three: that lupuric acid may possibly be synthesized elsewhere in the body besides the liver; that physiologic variations in the state of the liver at the time of the test may influence the results apart from the effects of true liver damage; and that renal damage may affect the quantity of hippuric acid excreted.

Although the Quick test can be performed satisfactorily by oral administration of the required amount of sodium benzoate, the dose occasionally tends to induce vomiting. Sometimes, too, an estimation of liver function is desired in a patient who is unable to take fluids by mouth. The intravenous method therefore is frequently of value; it is conducted as follows:

(a) Breakfast of toast and coffee is given at 7 A.M., or may be omitted if the patient cannot take food, and the urinary bladder is emptied.

(b) At 8 A.M., 20 c.c. of a sterile aqueous solution containing 1.77 Gm. of sodium benzoate (equivalent to 1.5 Gm. of benzoic acid) is slowly injected intravenously, the procedure occupying at least five minutes.

(c) The bladder is emptied again at 9 A.M., either by spontaneous voiding or by catheterization, and the specimen is saved, together with all the urine that may have been voided in the interval between 8 and 9 A.M.



(d) The volume of urine is measured, and 5 Gm. of solid ammonium sulfate is added for each 10 c.c. of urine. After the salt has dissolved, the urine is filtered by suction. Concentrated hydrochloric acid is added slowly to the filtrate until it is sufficiently acid to turn Congo red test paper blue. The solution is shaken vigorously for several minutes and is allowed to stand for half an hour to insure complete precipitation of the hippuric acid. The mixture is then filtered and the precipitate is washed, dried either in air or in an incubator, and weighed, a similar piece of filter paper being used for a counterbalance.

The total weight of hippuric acid excreted during the test is the net weight of the precipitate plus the quantity remaining in solution, which amounts to 0.1 Gm. for each 100 c.c. of urine containing 50 Gm. of ammonium sulfate. Normal excretion of hippuric acid in the adult should amount to approximately 10 gram. The degree of liver function may be reported as the percentage of this standard value. The quantity of hippuric acid obtained may be converted to its equivalent of benzoic acid by multiplying by the factor 0.68. Average normal excretion of benzoic acid under the circumstances of the test therefore amounts to 0.68 gram. The laboratory report should state which method of calculation is used.

The oral test, modified from Quick,<sup>4</sup> is performed in the same manner as the intravenous test, except that the patient is given 5.9 Gm. of sodium benzoate dissolved in 30 c.c. of water, flavored with cherry syrup. One-half glass of water is then given from the same glass used to administer the dose of sodium benzoate to make certain that all the drug is taken. No food or fluid of any kind is then permitted until after the test has been completed.

The patient voids immediately after taking the dose, and the specimen of urine is discarded. All the urine voided during the next four hours and at the end of this period (8 A.M. to 12 M.) is saved as a single specimen. If the patient cannot void at the end of the four-hour period, catheterization must be done at this time. It is evident that the success of the test depends upon proper collection of the urine specimens.

Determination of the quantity of hippuric acid excreted is done as previously described. If the total volume of urine collected exceeds 500 c.c., it may be concentrated to this amount by boiling, after acidification with acetic acid. The normal value for the oral

test is 3.0 Gm. of benzoic acid, and for the intravenous test, 0.68 gram. Expressed simply as hippuric acid, the normal value for the oral test is 4.4 Gm. and for the intravenous test, 1.0 gram.

Probably the simplest method of reporting the result of the Quick hippuric acid excretion test is in the form of percentage of normal quantity excreted. The test may be interpreted clinically as follows: values of 70 per cent or above indicate satisfactory liver function as far as this test can determine; values below these levels indicate moderate to severe degrees of liver damage, and operation should not be performed without intensive pre-operative preparation.

6. The *cephalin-cholesterol flocculation test*<sup>5</sup> is based upon the fact that liver damage causes qualitative alterations in the plasma proteins, particularly depression of serum albumin and increase in serum globulin (especially the gamma-globulin fraction).<sup>4</sup> A standard emulsion of cephalin and cholesterol will produce no effect upon normal serum but will cause flocculation and precipitation in the serum of a patient with depressed hepatic function, the flocculation reaction being proportionate to the alterations in serum protein and therefore to the degree of liver damage. The test is commonly reported as negative or as positive 1 plus to 4 plus, the extent of reaction in repeated tests roughly paralleling the progression or subsidence of hepatic disease.

7. The *thymol turbidity test*, introduced by Maclagan,<sup>7</sup> does not test any known specific function of the liver but apparently depends upon a somewhat similar mechanism to the cephalin flocculation reaction. It indicates a disturbance in hepatic metabolism rather than a depression in function and is especially useful in following the course of such liver diseases as hepatic cirrhosis and infectious hepatitis. The thymol turbidity test is probably best used in conjunction<sup>8</sup> with the cephalin flocculation test.

8. When liver function is seriously impaired, *prothrombin synthesis* may be deficient. Ivy and Roth<sup>8</sup> have suggested the parenteral administration of vitamin K in therapeutic doses for several days; if hypoprothrombinemia is noted in spite of this therapy, a serious degree of liver damage is present.

Since no liver function test affords dependable information on more than a single aspect of liver function, it is best to per-

for in several types of tests<sup>10</sup> before conclusions are drawn. The bromsulfalein, rose bengal, and galactose tolerance tests may be normal even in the presence of relatively advanced disease, the cephalin-cholesterol flocculation and the hippuric acid excretion tests are probably the most sensitive and the most informative of the commonly used tests of liver function.

Liver function tests should be repeated during the period of preparation until it is apparent that the liver function has attained its maximum improvement and during the postoperative period to detect any evidence of failing hepatic reserve.

Examination of the blood should include red cell count, hemoglobin determination, and white cell count, both total and differential. In the presence of severe hepatic parenchymal damage, the erythrocytes sometimes show macrocytosis. The chemical constituents of the blood show no constant significant alteration, except for the variations in serum bilirubin and in plasma proteins, including prothrombin. The clotting mechanism of the blood must be investigated in all patients who exhibit disease of the biliary tract, whether or not jaundice is present (p. 219). If any significant degree of anemia is noted, the patient is given transfusions of whole blood before operation until the hemoglobin reaches a minimum of 80 per cent (11.7 Gm.) and the red cell count reaches at least 4,500,000 per cubic millimeter. Hypoproteinemia due to malnutrition may be corrected by a high dietary intake of protein supplemented with transfusions of whole blood.

**Improvement of Liver Function.**—Previous note has been made of the parenchymatous liver changes consequent to malnutrition or to liver damage (p. 55). The glycogen content of the hepatic cells is decreased and the fat content increased as a result of deleterious influences of any kind. The liver glycogen not only serves as a store of labile carbohydrate, but also protects the hepatic cells from the effects of toxic agents and therefore *must be maintained at as high a level as possible*. While the glycogen stores of a fat-laden liver can be increased somewhat by the administration of large quantities of carbohydrate, the addition of a lipotropic substance to the diet is necessary to reduce the liver fat and improve the liver function. Ravdin and associates<sup>11</sup> have emphasized the use of a high

caloric diet containing a large proportion of carbohydrate and protein and very little fat. The diet which they have found most satisfactory contains carbohydrate, 70 to 80 per cent; protein, 20 to 30 per cent; and fat, 5 to 10 per cent. This diet can be supplemented every three or four hours during the day with intermediary nourishments containing an ounce or more of skim milk powder, casein, lactalbumin, or an oral preparation of protein hydrolysate. Fats such as chocolate, eggs, and cream should not be added to these feedings since a low fat intake is desired; also, fats are retained in the stomach for relatively long periods and decrease the appetite. Carbohydrates such as dextrose or Dextrimaltose may be added, however; these sugars are well absorbed and are not as sweet as sucrose. Vitamin preparations containing adequate therapeutic amounts of vitamin C and the vitamin B complex are similarly indicated. Although there is suggestive evidence that methionine and choline may be of value in improving deficient liver function (p. 57), clinical proof is not yet available. These substances apparently are of most value in patients with chronic liver disease, such as cirrhosis.

Patients who are unable to take sufficient food by mouth can be fed by stomach tube, with supplementary infusions, or can be fed entirely by infusion if necessary. Protein hydrolysate (5 per cent) in dextrose (5 per cent) administered intravenously in a quantity of 1,000 c.c. twice each day (p. 76) will supply approximately 100 Gm. of protein and 100 Gm. of carbohydrate. A patient who is ill enough to require this type of feeding will probably also require transfusions of whole blood. It is worth noting that additional salt in the form of normal salt solution is unnecessary if the protein hydrolysate preparation being employed contains sufficient sodium chloride to supply from 4 to 6 Gm. each day.

Oral feeding of carbohydrate, when possible, is probably as effective in restoring liver glycogen as is dextrose given intravenously. Since administration of sugar by mouth is simpler than administration by vein, full advantage should be taken of this method whenever possible.

The patient, if ambulatory, is weighed every other day before breakfast and the weight recorded.

**Preparation of Jaundiced Patients.**—The presence of jaundice is a complicating factor because of the increased liver damage usually present in such patients and the marked tendency to hemorrhage, especially after operation, characteristic of certain jaundiced subjects. Liver function is especially impaired following obstructive jaundice because of the heightened back pressure throughout the entire biliary tree, often exceeding the intrahepatic capillary pressure, and also because of the retention of toxic products. Operation upon a patient who exhibits obstructive or toxic jaundice is always potentially if not actually dangerous and is never to be undertaken without preparation except as an emergency procedure. Several days must be spent in preparation even if the jaundice is growing deeper. Carbohydrates are given in large quantities both orally and intravenously to jaundiced patients. At least 500 Gm. of carbohydrate a day should be administered by these routes, and an intravenous infusion of dextrose (10 per cent) solution is especially indicated just before and again immediately after operation.

The type, degree, and progress of the jaundice are determined by clinical and laboratory studies.<sup>22</sup> Serum bilirubin and icteric index determinations are made, a van den Bergh test is performed, and examinations of the urine and stool for bile and urobilinogen are done. In general, jaundice of the *obstructive* type is characterized by a direct van den Bergh reaction, an elevated serum bilirubin and icteric index, the absence of bile in the stool, and the presence of large quantities of bile in the urine but no urobilinogen. Since no bile reaches the intestinal tract, no urobilinogen is formed. Jaundice of this type may be intense and is often characterized by severe itching, which may appear even before the icterus becomes visible. Jaundice of the *toxic* type usually develops in a patient who is more severely ill, and clinically resembles obstructive jaundice except for the facts that the van den Bergh test may be biphasic and bile is present in the stool as well as in the urine. In this type of liver disease, depressed excretory power of the liver cells and areas of parenchymal hepatic necrosis are both present. Jaundice of the *hemolytic* type, on the other hand, is never so intense as that secondary to obstruction of the bile ducts; the van den Bergh test is typically indirect, and bile is present in the stool in large quantities but absent from the urine, although urobilinogen can

he found in the urine. Large quantities of bilirubin are formed by destruction of red blood cells, and the physiologic capacity of the liver to excrete the excess may be temporarily overtaxed. A high level of bilirubin therefore is present in the circulating blood for a variable length of time. Because of the excessive bilirubin production and excretion, an unusually large amount of urobilinogen is formed in the intestine; urobilinogen consequently appears in increased amounts in the stool and in the urine. However, since there is no regurgitation of excreted bile from the biliary tract, no bile is found in the urine in hemolytic jaundice. Hemolytic jaundice can be diagnosed with certainty by the presence of acholuric jaundice and by the demonstration of increased fragility of the erythrocytes, large numbers of which appear as small abnormally spherical forms (spherocytes).

Patients with familial hemolytic jaundice usually show pronounced anemia, decreased total blood volume, and impaired liver function. The occurrence of acute hemolytic crises also is a characteristic feature of this disease. Splenectomy is the treatment of choice, but operation is not advisable during the course of an acute crisis. Transfusion of blood, usually employed pre-operatively to replace the destroyed red cells, sometimes appears actually to induce an acute crisis, with deterioration rather than improvement in the patient's condition. The suggestion therefore has been made<sup>23</sup> that administration of plasma rather than of whole blood will produce temporary improvement by increasing the total blood volume without danger of initiating hemolysis.

**Hemorrhagic Tendency.**—Certain patients with obstructive jaundice are likely to exhibit a severe hemorrhagic tendency because of hypoprothrombinemia. Prothrombin, a necessary component of the clotting mechanism of the blood, is synthesized by the liver under the influence of vitamin K, which is absorbed from the diet through the gastrointestinal tract. Since this substance is fat soluble, exclusion of bile from the intestine by the obstructive process responsible for the jaundice will result in failure of absorption of fats and consequent deficiency of vitamin K and therefore in deficient synthesis of prothrombin.<sup>12</sup> The hemorrhagic tendency may be measured by the Quick prothrombin time test or some modification thereof (p. 221) and proper

therapy instituted when a dangerous hypoprothrombinemia is present.

Little prolongation of clotting time is noted until the prothrombin concentration of the blood has dropped to 20 to 30 per cent of normal or below, although the time required for clot formation increases rapidly after that point. Since the available prothrombin may be utilized in the coagulation of exudate in the operative region during and immediately after operation, hemorrhage may occur postoperatively when the preoperative prothrombin level is close to the danger point. In general, if the prothrombin time is above 25 seconds, or if the prothrombin concentration is below 40 per cent of normal, the patient is definitely a potential bleeder.

Prothrombin deficiency is treated by administration of vitamin K or rather of synthetic compounds with a high vitamin K activity. Extracts of the vitamin K occurring naturally in alfalfa have shown it to consist of several closely related naphthoquinones, the simplest and most active of which is 2-methyl-1,4-naphthoquinone (menadione). This substance, available as a synthetic preparation, is insoluble in water and must be given orally. Doses of 1 to 2 mg. daily are used, with simultaneous administration of bile salts, 0.3 to 0.6 Gm. (gr. 5 to 10), accompanying each dose to insure proper absorption from the bowel. The concomitant use of bile salts is especially necessary when the patient is jaundiced. If oral administration is impossible or undesirable, or if a more rapid effect is necessary, a water-soluble derivative of menadione can be given intramuscularly or intravenously; for example, menadione-sodium bisulfite. The effective dosage of the soluble form is approximately twice that of simple menadione, from 2 to 5 mg. being administered once daily. Larger doses are not necessary and should not be used; the only indication for a larger amount is in treatment of dicumarol overdose (p. 392), in which the prothrombin of the blood has been reduced to a dangerously low level.

Menadione and its soluble derivatives<sup>12</sup> produce a rapid and rather prolonged effect; a single dose of 2 mg. may elevate a low prothrombin level by as much as 40 per cent and sustain it for several days. The effect is noticeable within several hours after oral administration of the drug and within less than an hour when it is given parenterally.

Hypoprothrombinemia due to deficiency of vitamin K is the only type of prothrombin deficiency that responds to treatment with natural or synthetic vitamin K. Prothrombin deficiency as a result of decreased liver function or marked liver damage (for example, in cirrhosis, toxic hepatitis, or hepatic carcinoma) will not respond to vitamin K therapy. In such patients transfusions of fresh blood and general measures to improve the liver function will usually produce a favorable response.

Severe prothrombin deficiency and a well-marked hemorrhagic tendency may exist in the absence of jaundice. Proper synthesis of prothrombin by the liver depends upon four factors: (1) adequate amounts of vitamin K in the diet, (2) the presence of bile in the intestine, (3) a normally absorptive intestinal surface, and (4) a physiologically adequate liver. For these reasons, a patient who has been on a severely restricted diet, who exhibits pyloric obstruction, or who has a biliary fistula is likely to exhibit a prolonged prothrombin clotting time even in the absence of jaundice and therefore may require specific therapy before operation can be undertaken safely.

The prothrombin concentration should be brought to at least 75 per cent of normal before operation is performed. Administration of vitamin K must be continued after operation and throughout the postoperative period as long as prothrombin deficiency exists, until the patient is able to take an adequate diet by mouth. The tendency of patients with drainage tubes in the gall bladder or biliary tract to develop hypoprothrombinemia as a result of the diversion of bile must be remembered.

**Biliary Colic.**—The use of morphine in the treatment of biliary colic is contraindicated except as a last resort. By inducing a spasm of the sphincter of Oddi, the drug may produce a marked and sustained rise in intraductal pressure throughout the entire biliary tree and consequently add to the degree of hepatic damage. Relief of pain is due to the central action of the opiate, and large doses of 24 to 32 mg. (gr.  $\frac{3}{8}$  to  $\frac{1}{2}$ ) are generally necessary. Since the colicky pain is caused by smooth muscle spasm behind the intraductal obstructing foreign body, relief of the spasm will accomplish relief of pain. A tablet of nitroglycerin, 0.6 mg. (gr.  $\frac{1}{100}$ ), may be placed beneath the tongue, or an ampule of amyl nitrite may be broken in a hand-



kerchief and inhaled. The transient but rapidly effective action of these drugs may be reinforced by the simultaneous administration of atropine, 0.6 (gr. 1/100), hypodermically. Aminophylline, administered slowly by vein in doses of 0.24 to 0.48 Gm. (gr. 3 3/4 to 7 1/2), is often effective in relieving the pain of biliary colic. The larger dose, when necessary, is best given dissolved in 100 c.c. of normal salt solution and administered by intravenous drip. Meperidine (Demerol) also may prove more satisfactory than morphine, since it combines analgesic and antispasmodic effects; it is given intramuscularly or orally in doses of 100 to 200 mg. for biliary colic. Immersion of the patient in a tub of warm water sometimes relieves lesser degrees of biliary or renal colic. Administration of tetraiodophenolphthalein to these patients for cholecystography may initiate a fresh attack; this diagnostic measure should be omitted in such cases.

**Summary.**—A patient who enters the hospital for an operative procedure upon the biliary tract will probably exhibit some degree of parenchymal liver damage and perhaps impairment of function of other viscera. Thorough investigation of cardiac and renal reserve should be made and the blood studied for evidence of anemia. The degree of liver damage can be estimated by clinical tests, particularly by means of the cephalin-cholesterol flocculation test and the Quick hippuric acid excretion test, which should be repeated at frequent intervals during the preoperative and early postoperative periods. Cholecystograms may be secured by roentgenologic visualization of the gall bladder following ingestion of tetraiodophenolphthalein, this procedure serving also as a dependable test of liver function, although it should not be used in the presence of jaundice or of severe visceral disease. If jaundice is present, the type and degree should be determined by appropriate laboratory procedures, and the presence of a hemorrhagic tendency should be determined by repeated estimations of the prothrombin clotting time.

When the physiologic status of the patient has been determined, efforts are made to repair the visceral damage before operation, which is delayed until repeated tests of hepatic function and prothrombin clotting time demonstrate that the patient has reached a peak of improvement. As long as jaundice is decreasing and improvement is continuing, operation is deferred;

when the jaundice has disappeared or has become stationary, surgery may be undertaken with a maximum of safety. Even if jaundice is increasing, several days may profitably be spent in attempts to improve the function and reserve of the damaged liver.

Indispensable preoperative preparatory measures include transfusion of fresh whole blood until the hemoglobin is elevated to 80 per cent or more, administration of fluids either orally or parenterally until dehydration has been corrected, and institution of a high caloric, high vitamin diet. A damaged liver, low in glycogen and high in fat content, is extremely susceptible to injury, while a liver high in glycogen and low in fat content is highly resistant to toxic influences. An appropriate diet therefore should contain 70 to 80 per cent carbohydrate, 20 to 30 per cent protein, and 5 to 10 per cent fat, with supplementary nourishments of simple protein or protein hydrolysate and added carbohydrates both orally and intravenously. Vitamin concentrates of A, B complex, and C are administered in therapeutic doses. In the presence of jaundice, determinations of prothrombin concentration and clotting time are made repeatedly; if a deficiency of any significant degree is noted, specific therapy with vitamin K is instituted and is continued during the early postoperative period.

### Postoperative Care

After the patient has recovered from the anesthetic, the bed is placed in the horizontal or the low Fowler position, and the dressing is inspected to make sure that it is not so tight as to interfere with respiration. An infusion is ordered immediately upon the patient's return to the ward. During the first day or two after operation, fluid balance is maintained by the intravenous administration of dextrose (5 per cent) solution in quantities of 2,000 to 3,000 c.c. daily, with transfusions of blood as required. Following the immediate postoperative period, normal salt solution is used in amounts not exceeding 1,000 c.c. daily unless chloride loss or hypochloremia is present; the remainder of the fluid requirement is supplied as dextrose (5 per cent) solution or protein hydrolysate (5 per cent) solution. Fluids by mouth are withheld during the first twenty-four hours, and a sur-

gical liquid diet is given on the second day. Adequacy of fluid intake is probable if the daily output of urine amounts to 1,000 to 1,500 cubic centimeters.

If the patient shows evidence of shock following operation, a transfusion of whole blood is given immediately. Blood loss during operations on the biliary tract may range from as little as 200 c.c. to as much as 1,500 c.c., with an average loss of about 600 c.c. (p. 160). This lost blood is best replaced by transfusion during operation; if not, it should certainly be restored immediately afterward. The danger of development of postoperative pulmonary atelectasis and pneumonia can be decreased by the administration of carbon dioxide (5 per cent) in oxygen every one to two hours for the first twenty-four to forty-eight hours, by institution of deep-breathing exercises, and by changing the patient's position every two hours when he is awake. The development of postoperative thrombophlebitis should be discouraged by the institution of exercising movements of the legs after the day of operation. Oxygen may be of great value in liver damage.

Administration of vitamin K (menadione) must be continued as long as the prothrombin level is dangerously low. Since the postoperative diet is necessarily restricted, hemorrhage may occur even as late as the twelfth day in the presence of prothrombin deficiency. Particular attention must be paid in this respect to patients whose bile is diverted from the intestine by a drainage tube in the gall bladder or common duct. Hemorrhage on this deficiency basis does not ordinarily require operative control but will cease spontaneously following administration of a transfusion of fresh blood with simultaneous intramuscular administration of a soluble menadiolone derivative in a dose of 2 to 5 milligrams.

**Uncomplicated Cholecystectomy.**—Following simple removal of the gall bladder, the course usually is relatively uncomplicated. If the gall bladder is removed gently during the operation, there will probably be little subsequent nausea; if the contents are squeezed into the duodenum and prolonged tension exerted upon the hepatoduodenal ligament, postoperative nausea and vomiting may be severe as a result of the excessive reflex stimulation. Drains are loosened forty-eight hours after operation, partially withdrawn on the next day, and re-

moved completely on the following day. Leakage of moderate amounts of thin, bile-stained fluid may occur during the first few days after operation from the traumatized bile canaliculi in the gall bladder bed.

**Cholecystostomy.**—Drainage of the gall bladder by means of a rubber tube is usually established in patients who are too ill to endure a more taxing operation or who have chronic or acute pancreatitis. These patients tend to pass a relatively stormy postoperative course because of the diversion of bile from the gastrointestinal tract and the consequent reduction in pressure throughout the biliary duct system. Digestion is impaired and nausea, vomiting, and intestinal distention may be marked.

When the patient is returned from the operating room, the gall bladder drainage tube is connected to a bottle at the bedside in such a way that the patient may move about without exerting traction on it. Flow of bile is usually free for the first few days, but as granulation occurs around the end of the tube and the catgut sutures begin to absorb, the discharge of bile progressively decreases and stops entirely after ten to fifteen days. The tube may be removed by gentle traction after sixteen days or will usually drop out spontaneously within eighteen to twenty days.

Since impairment of liver function is particularly likely to be prolonged following cholecystostomy,<sup>4</sup> special care must be taken that such a patient receives adequate amounts of fluids and carbohydrates following operation. The degree of hepatic damage and rate of recovery should be checked at intervals after operation by means of the Quick hippuric acid and cephalin-cholesterol flocculation tests and any tendency to the development of hypoprothrombinemia noted by determinations of the prothrombin clotting time.

**Choledochostomy.**—Drainage of the common bile duct by means of a catheter or a T tube is performed in association with operations upon the common duct for removal of stones or reconstruction of strictures. When the patient is returned from the operating room, the drainage tube is unclamped and inserted into a bottle attached to the side of the abdominal binder in such a way that the open end of the tube is approximately at or slightly above the level of the common bile duct (Fig. 72). Spillage may be prevented by passing the tube through a rubber

nipple, which is then attached over the mouth of the drainage bottle. A tiny hole should be cut in the nipple to allow the escape of air from the bottle as it fills with bile. Drainage into a bottle below the level of the bed is not recommended, since the constant siphonage of bile from the biliary ducts which occurs by this method reduces the pressure throughout the biliary tree to such a point that hepatic damage may ensue. Also, siphonage

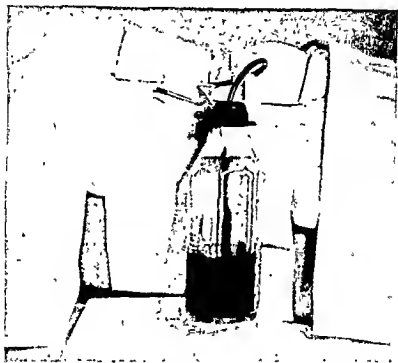


Fig. 72 —Collecting apparatus for use following common bile duct drainage. The collecting bottle is attached to the dressing at such a level that the end of the drainage tube is slightly above the level of the common bile duct. To prevent spilling, the tube is passed through a rubber nipple with a small additional air hole. A Hoffman clamp can be applied to the tube to regulate the rate of drainage. The bottle can be unplugged and reattached as the patient changes position. A smaller bottle can be used as the amount of drainage decreases.

of bile in this way will interfere with drainage of bile into the duodenum even though the common duct is patent. Raydin and Frazier<sup>14</sup> have described an apparatus which permits adequate biliary drainage and yet maintains a satisfactory back

pressure in the duct system. Although the reported method is effective and physiologically sound, the same purpose perhaps may be served sufficiently well by controlling the rate of drainage by means of a Hoffman clamp if necessary.

The bile is allowed to drain freely during the first three days after operation, and then, if progress of the patient is satisfactory, the tube may be clamped off for an hour or two each day. If the common duct is clear and the sphincter of Oddi not unduly spastic, the intraductal pressure, heightened during the time the drainage tube is closed off, will force the bile into the duodenum. The tube may be clamped for successively longer periods if there is no untoward reaction. Pain occurring shortly after the tube is clamped indicates that duodenal drainage is blocked and that the biliary tract is distended with retained bile. Obstruction due to spasm or edema of the sphincter usually disappears a few days after operation and bile then drains into the duodenum without difficulty. Although some surgeons have suggested collection of the discharged bile and its reintroduction into the duodenum by means of a stomach tube, the drainage is usually measured, examined, and discarded, and water-soluble animal bile is administered orally or by tube in amounts of 0.6 to 1.0 Gm. (gr. 10 to 15) several times daily until it is no longer necessary.

The average daily output of bile from a tube in the common duct amounts to 300 to 500 c.c., although larger quantities may be excreted during the first few days after operation. This loss of fluid and electrolytes should be noted on the fluid balance sheet and equivalent amounts of normal salt solution added to the daily fluid intake required. Measurement of the biliary drainage is important, and this source of fluid loss must not be overlooked.

Carter<sup>18</sup> points out that the flow of bile during the night may be diminished by giving the patient a small quantity of food at midnight. He also suggests that the physiologic response of the sphincter of Oddi may be tested by measurement of the biliary output before and after meals. The amount of bile discharged into the drainage bottle should be measured each hour during the day, care being taken to keep the open end of the T tube at or above the level of the common duct to avoid siphonage. If the sphincter of Oddi is functioning normally, bile will flow

into the duodenum following the ingestion of food, while if it is spastic, an unusually large quantity of bile will be excreted into the drainage bottle at this time. Spasm of the sphincter can be differentiated from organic occlusion of the duct by the administration of atropine, 0.6 mg (gr. 1/100), hypodermically or nitroglycerin, 0.6 mg. (gr. 1/100), beneath the tongue. Either drug will tend to relax a spastic sphincter and will consequently encourage the flow of bile into the duodenum, decreasing the quantity of external drainage, while neither drug will produce any effect in the presence of organic occlusion of the bile ducts. Such a test should be made if interference with biliary drainage into the duodenum is prolonged more than the usual four to seven days after operation.

**CHOLANGIOGRAPHY.**—After the postoperative febrile reaction has disappeared, usually by the tenth day, a cholangiogram may be secured to confirm the patency of the common duct. The day before the x-ray is to be taken, the duct should be flushed with small amounts of sterile normal salt solution, which should be injected without much pressure and aspirated back. For visualization of the common duct, the bile is first aspirated and then a warm sterile aqueous 48 per cent solution of Hippuran is introduced, amounts of 10 to 25 c.c. usually being sufficient. If pain occurs during introduction of the radiopaque material, injection should be stopped; such pain is ordinarily due to distention of the biliary tract under pressure. A roentgenogram is made as soon as the required amount of solution has been introduced, another is made in three to four minutes, and a final picture is taken after ten minutes, at which time all of the dye should be in the duodenum. The cholangiogram should show the biliary ducts to be unobstructed and of normal size, without dilatation. Best<sup>16</sup> advocates the use of Hippuran solution rather than iodized oil, since the heavier liquid may obscure the presence of small stones. If iodized oil is employed, it should be diluted 2:1 with sterile olive oil and warmed to body temperature.

**REMAINING STONES.**—Colicky pains after operation upon the common duct may indicate the presence of small remaining stones, and silent stones can sometimes be visualized by cholangiogram. These calculi should be dislodged if possible by such nonoperative methods as the plan devised by Best and Hicken.<sup>17</sup>

These authors suggest the following three-day program, both for nonoperative removal of demonstrable common duct stones and for relief of the colicky pains which sometimes follow any operative procedure upon the biliary tract.

1. *First day.* Nitroglycerin, gr. 1/100 (0.6 mg.), administered beneath the tongue three times, in order to relax the sphincter of Oddi (morning, afternoon, and evening).

2. *Second day.* Atropine, gr. 1/100 (0.6 mg.), either orally or hypodermically three times.

3. *Third day.* Nitroglycerin, gr. 1/100 (0.6 mg.), administered beneath the tongue three times.

The patient is given 8 Gm. of magnesium sulfate in warm water each morning and 1 ounce of olive oil or thick cream each night. The common duct is irrigated gently once a day through the T tube with warm sterile normal salt solution. This is re-aspirated and 10 to 30 c.c. of warm sterile olive oil injected. The tube is kept clamped off constantly except for thirty minutes following each instillation unless pain is caused by the increased intraductal pressure. In addition, bile salts, 0.6 Gm. (gr. 10), are given four times daily.

The rationale of the measure is that relaxation of the sphincter of Oddi is secured by means of the antispasmodic drugs and the substances by mouth, while the flow of bile is increased by the cholagogue effect of bile salts. Attempts to wash out the stone by vigorous irrigation through the catheter are unwise, since the foreign body may thereby be forced up toward the liver.

Obviously, this procedure cannot be used in the presence of complete obstruction of the common duct, and the presence of even a slight degree of persistent jaundice contraindicates the clamping of the drainage tube. If the program is unsuccessful on the first attempt, it may be repeated after several days. The authors advise its use as a routine measure following any operation upon the biliary tract in which a T tube is used.

**REMOVAL OF THE T TUBE.**—The common duct drainage tube is allowed to remain in place until all evidence of cholangitis has disappeared. Microscopic examination of the bile collected from the tube is performed at frequent intervals during the post-operative course and again just before the tube is removed.



Search should be made on each occasion for pus cells, bile sand, and crystals of cholesterol, calcium bilirubinate, or calcium carbonate. As a rule, when drainage of the common duct has been instituted following removal of a stone in the absence of cholangitis, sterile pus will appear in small quantities for a few days as the result of irritation by the tube, but the pus cells will decrease rapidly in number until twelve to fourteen days after operation, when only an occasional white blood cell will be seen. Criteria for removal of the drainage tube, accomplished by gentle traction at this time, include (1) absence of pus or crystals on microscopic examination of the bile; (2) physiologic and unobstructed drainage into the duodenum as demonstrated by Carter's food test (p. 713) and physiologic response of the sphincter of Oddi to atropine; (3) satisfactory cholangiography; (4) presence of bile salts in the bile.

The persistence of cholangitis is evidenced by the presence of microscopic pus in the bile over a period of weeks or months. Crystals of calcium bilirubinate in the bile indicate the presence of chronic infection, precipitated pigment, and possibly tiny stones or organized sediment in the biliary tract. Cholesterol crystals, which usually disappear from the bile within a few days after operation, if persistent, may indicate the presence of a stone in the common duct overlooked at operation. Crystals of calcium carbonate are not often observed; their continued presence may be due to an associated pancreatitis. The T tube must not be removed from the common bile duct as long as any of these substances is present in significant amounts on microscopic examination of the bile or as long as the function of the sphincter of Oddi is in any way impaired. In some cases, evidences of chronic cholangitis may persist over a period of many weeks or months. Removal of the tube before the residual infection is cleared may result in clinical cholangitis or in the establishment of an external biliary fistula, while if the tube is retained until the bile is microscopically clear and drains into the duodenum without back pressure, the drainage tract will heal promptly after its withdrawal. Tincture of belladonna (10 drops) may be taken after each meal for a few days after the drainage tube is removed to assure proper relaxation of the sphincter of Oddi.

### Complications Following Biliary Tract Surgery

Because of the disturbed physiology consequent to disease of the biliary tract, operations upon the bile ducts are especially likely to be followed by complications. The usual precautions must be taken to prevent the development of postoperative atelectasis, pneumonia, thrombophlebitis, dehydration, acidosis, hypoproteinemia, or wound dehiscence, and the hepatic reserve must be fortified by the maintenance of a high carbohydrate and protein intake throughout the entire postoperative course. Besides the complications that may occur following any abdominal surgical procedure, there are several which are more or less characteristic after biliary tract surgery (Fig. 73).

**Postoperative hemorrhage**, particularly likely to occur in jaundiced patients or in association with external biliary drainage, is usually due to a deficiency in the prothrombin of the blood. A specimen of blood should be withdrawn immediately for determination of the prothrombin clotting time and a soluble menadione derivative given intravenously in a dose of 2 to 5 milligrams. A transfusion of fresh whole blood is administered if the hemorrhage is a significant one; the transfusion itself will supply sufficient prothrombin to halt the hemorrhage for several hours, but the lacking factor also must be supplied.

Bleeding from the operative field is rarely due to surgical causes. If the cystic artery has not been ligated separately, the ligature may slip off after operation, although this occurrence is very uncommon. Venous blood may ooze persistently from the damaged liver in the region of the gall bladder bed or from small veins in the mesocysticum or hepatoduodenal ligament. Such bleeding points may appear insignificant during operation when the patient's blood pressure is low and yet become potentially dangerous sources of continued blood loss when the blood pressure rises following operation. Persistent seepage of serosanguinous fluid around the drains or through the wound edges should arouse suspicion of internal bleeding, especially if the pulse is weak and rapid and the blood pressure fails to rise toward normal.

If the clotting mechanism of the blood is normal and administration of menadione and of one or two transfusions of fresh whole blood repeated at short intervals fail to stop the hemor-

rhage, the patient should be returned to the operating room for surgical control of the bleeding vessel without more delay.

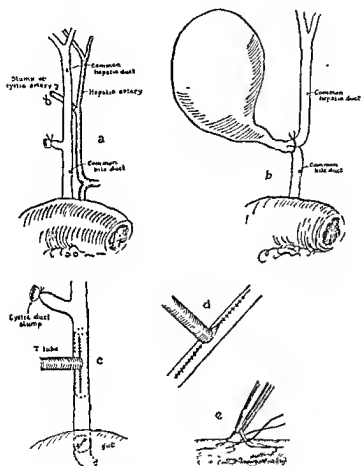


Fig 73—Technical errors in biliary tract surgery. *a*, Slipping of ligature on cystic artery, with postoperative hemorrhage. *b*, Inclusion of common bile duct in ligation of cystic duct, with postoperative obstructive jaundice. *c*, Overlooked stone in common duct, with postoperative obstructive jaundice. *d*, Improper closure of common duct incision, with postoperative leakage of bile. *e*, Injury to common bile duct during ligation of small vessel, with subsequent slough and leakage.

Injury to the common bile duct or common hepatic duct may occur as a result of the inadvertent and unrecognized inclusion of these structures in the ligature around the cystic

duct during the course of a cholecystectomy. Sometimes, too, a clamp and ligature improperly applied to a free and actively bleeding cystic artery may include the hepatic duct, with resultant obstruction. Either of these accidents will be followed within a day or two by the rapid development and progression of a painless obstructive jaundice, with acholic stools and bile in the urine, and a subsequent external biliary fistula. The diagnosis is always obvious, and the obstruction should be corrected surgically at once, with drainage of the common duct by means of a T tube to prevent subsequent stricture formation. If the diagnosis is not made until after several days have passed, it is best to delay repair<sup>18</sup> until after the postoperative edema and inflammatory response have subsided. A delay of several months is advisable if an external biliary fistula develops, if obstructive jaundice without fistula develops, repair should be undertaken within several weeks.

Postoperative obstruction of the common bile duct may occur from several other causes. Excessive dilatation of the ampulla with metal probes or dilators may cause trauma and tearing of the sphincter of Oddi, with paralysis and incompetence for a few days and later scarring, fibrosis, and stricture. Similar damage of a less severe degree may be followed merely by a prolonged postoperative edema of the ampullar sphincter. For these reasons, progressive dilatation of the ampulla, once its patency has been established, is no longer generally practiced.

A stone in the common duct, overlooked at operation, may result in postoperative obstruction of the duct between the drainage tube and the ampulla. The presence of such a calculus should be suspected if complete obstruction to the flow of bile into the duodenum continues for more than two weeks after operation, since simple postoperative edema or spasm of the ampullar sphincter usually disappears within five to ten days. *Differential diagnosis* may be made by means of a cholangiogram. If a stone is actually present, repeated efforts should be made to dislodge it by nonoperative means (p. 715). Secondary operation, although attended by a high mortality, is the only resource if the stone cannot be made to pass into the duodenum by means of antispasmodic medications. A drainage tube should never be removed from the common bile duct before a cholangiogram

has been secured and satisfactory drainage into the duodenum demonstrated.

Improper closure of the common duct around the drainage tube or inclusion of a segment of the common duct wall in a ligature with subsequent sloughing may permit leakage of bile into the general peritoneal cavity, with biliary peritonitis resulting. Marked irritative symptoms will develop, and fresh bile may be observed on the dressings over the abdominal wound. Nausea and vomiting are severe and persistent, and intestinal distention appears, occasionally progressing into paralytic intestinal obstruction. The necessity for operative correction of the leak depends upon the individual case; nonoperative management is similar to that advised for paralytic intestinal obstruction from any other cause (p. 440). Conservative treatment is the most satisfactory course if an external biliary fistula develops promptly.

Liver failure has received much attention from both the clinical and the experimental points of view and is believed to be an uncommon but a possible cause of death following surgery on the biliary tract as well as following other types of surgery. It has already been remarked that reduction of liver function may exist in the absence of clinical evidence, and the consequent necessity for investigation of hepatic function before operation has been stressed. The methods by which liver function can be improved also have been outlined.

So-called "liver deaths," which were first described by Heyd<sup>18</sup> in 1924, are classified into two general groups. In the first group there is a delayed recovery from the anesthetic; a semicomatose state ensues, and death occurs within eighteen to forty-eight hours, with hyperpyrexia as the outstanding symptom. The only notable autopsy finding is necrosis of the liver cells.

*In the second type death is delayed for ten to fourteen days or even longer. Convalescence is satisfactory or good for the first five or six days and recovery is apparently progressing well when suddenly the patient becomes somnolent, progressively deepening coma develops, and death occurs within a short time thereafter. In this group of cases a deferred renal factor, which becomes clinically evident as oliguria and often progresses to*

complete anuria, is in sharp contrast to the hyperpyrexia which is the outstanding feature in the first group. In the uremic type of death (the so-called liver-kidney syndrome) a necrotic process is found in the convoluted tubules of the kidney as well as in the liver.

Boyce and McFetridge,<sup>20</sup> Helwig and Schutz,<sup>21</sup> and others who have worked extensively on this problem are inclined to believe that both types of liver death are manifestations of the same pathologic process. According to Boyce and McFetridge, a subclinically damaged liver may function adequately under the ordinary circumstances of life but will fail under the added load imposed by anesthesia, surgical trauma, and the direct hepatic damage which necessarily follows any type of operation on the biliary tract. The products of metabolism, which ordinarily are detoxified in the liver, accumulate in the body, and additional toxic products are probably released as the result of autolytic changes in the parenchymal cells of the failing liver. The increasing amounts of toxins from both of these sources, if they do not promptly overwhelm the patient, must be excreted by the kidneys, the reserve capacity of which is quickly exceeded, so that death inevitably follows. Helwig and Schutz offer the same explanation except that they believe that the toxin elaborated in the necrotic hepatic tissue has a specific action on the renal parenchyma.

It must be added that the existence of the liver death or hepatorenal syndrome is denied by many surgeons and that only complete post-mortem observations can supply valid proof that it is the cause of death in any given case.

For these reasons, when liver damage is noted to be present by preoperative tests of hepatic function, the deficiency must be corrected, chiefly by the simple administration of sugar and readily assimilable protein, both orally and intravenously. If hepatic deficiency continues into the postoperative period or is suspected or demonstrated at this time, the same simple procedure will usually prove effective in warding off hepatic or hepatorenal failure.

## References

1. Kolmer, J. A., and Boerner, F.: *Approved Laboratory Technic*, ed 4, New York, 1945, D Appleton-Century Co., Inc.
2. Macdonald, D.: *A Practical and Clinical Test for Liver Reserve*, Surg. Gynec. & Obst. 69: 70, 1939.
3. Quick, A. J.: Intravenous Modification of the Hippuric Acid Test for Liver Function, *Am. J. Digest Dis.* 6: 716, 1939.
4. Boyce, F. F., and McFetridge, E. M.: Studies in Hepatic Function by the Quick Hippuric Acid Test. I. Biliary and Hepatic Disease, *Arch. Surg.* 37: 401, 1938.
5. Hanger, F. M.: Serologic Differentiation of Obstructive From Hepatogenous Jaundice by Flocculation of Cephalin Cholesterol Emulsion, *J. Clin. Investigation* 18: 261, 1939.
6. Moore, D. H., Pierson, P. S., Hanger, F. M., and Moore, D. H.: Mechanism of the Positive Cephalin Cholesterol Flocculation Reaction in Hepatitis, *J. Clin. Investigation* 24: 296, 1945.
7. MacLagan, N. F.: The Thymol Turbidity Test as an Indicator of Liver Dysfunction, *Brit. J. Exper. Path.* 25: 234, 1944.
8. Recant, L., Chergaff, E., and Hanger, F. M.: Comparison of the Cephalin-Cholesterol Flocculation With the Thymol Turbidity Test, *Proc. Soc. Exper. Biol. & Med.* 60: 245, 1945.
9. Ivy, A. C., and Roth, J. A.: Why Do a Liver Function Test? *Gastroenterology* 1: 655, 1943.
10. Allen, J. G.: The Clinical Value of the Functional Tests of the Liver, *Gastroenterology* 3: 490, 1944.
11. Ravdin, I. S.: *Surgical Diseases of the Extrahepatic Bile Ducts*, New England J. Med. 220: 326, 1939.
12. Quick, A. J.: *The Hemorrhagic Diseases and the Physiology of Hemostasis*, Springfield, Ill., 1942, Charles C Thomas.
13. Richards, R. K., and Shapiro, S.: Experimental and Clinical Studies on Action of High Doses of Hykinone and Other Menadione Derivatives, *J. Pharmacol. & Exper. Therap.* 81: 93, 1945.
14. Ravdin, I. S., and Frazier, W. D.: The Advantages of Gradual Decompression Following Complete Common Duct Obstruction, *Surg., Gynec. & Obst.* 65: 11, 1937.
15. Carter, R. F.: When to Remove Drainage Tube in Common Bile Duct Drainage, *Surg., Gynec. & Obst.* 63: 163, 1936.
16. Best, R. R.: Cholangiographic Demonstration of the Common Duct Stone and Its Non-Operative Management, *Surg., Gynec. & Obst.* 66: 1040, 1938.
17. Best, R. R., and Hicken, N. F.: Nonoperative Management of Remaining Common Duct Stones, *J. A. M. A.* 110: 1257, 1938.
18. Cattell, R. B.: Strictures of the Biliary Ducts, *J. A. M. A.* 131: 235, 1947.
19. Heyd, C. G.: The Liver and Its Relation to Chronic Abdominal Infections, *Ann. Surg.* 79: 55, 1924.
20. Boyce, F. F., and McFetridge, E. M.: So-Called "Liver Death." A Clinical and Experimental Study, *Arch. Surg.* 31: 105, 1935.

21. Helwig, F. C., and Schutz, C. B.: A Liver Kidney Syndrome. Clinical, Pathological, and Experimental Studies, Surg., Gynec. & Obst. 55: 570, 1932.
22. Young, L. E.: Medical Progress: Current Concepts of Jaundice, With Particular Reference to Hepatitis, New England J. Med. 237: 225, 261, 1947.
23. Pfeiffer, D. B., and Levering, J. W.: Familial Hemolytic Anemia and Its Surgical Aspect, With Special Reference to a Case Complicated by the Rh Factor, Ann. Surg. 126: 990, 1947.



## CHAPTER 22

# THYROID

### Etiology of Hyperthyroidism

There is still considerable uncertainty concerning the mode of development of hyperthyroidism and the etiologic factors involved. In particular, much discussion has arisen as to whether the manifestations of the toxic thyroid states are due to excess production of normal thyroid hormone or to secretion of a pathologic and chemically altered hormone, as well as to the parts played by other endocrine glands in the development of the more advanced degrees of hyperthyroidism.

The concept most generally recognized at present is that hyperthyroidism is due to excessive secretion of normal thyroid hormone. In toxic nodular goiter (adenomatous goiter), the hypersecretion probably arises in the nodules or in the parenchymal tissues immediately surrounding the nodules. Toxic diffuse (exophthalmic) goiter, on the other hand, has a more complicated origin; whatever the primary initiating factors may be, it is likely that the disease is due largely to hypersecretion of the thyrotropic (thyrotrophic) hormone originating in the anterior lobe of the pituitary gland. The excess amount of thyrotropic hormone produces increased stimulation of the thyroid parenchymal cells, with increased production of thyroxine.

Exophthalmic goiter, however, is characterized by signs and symptoms which cannot be explained<sup>1</sup> on the basis of thyrotoxicosis alone; manifestations such as exophthalmos probably are direct effects of the excessive anterior pituitary thyrotropic hormone. Certain experimental and clinical findings support these conclusions; administration of anterior pituitary hormone will cause thyroid hyperplasia, increased basal metabolic rate, and pronounced exophthalmos in various normal experimental animals. Administration of the pituitary principle to thyroidectomized animals will not elevate the metabolic rate but will produce an even more marked degree of exophthalmos,<sup>2</sup> which can be minimized by simultaneous administration of thyroid extract.

Similar conditions have been noted clinically; in Graves' disease the degree of exophthalmos is not always proportionate to the degree of thyrotoxicosis, advanced and intractable cases of proptosis occasionally being present in patients who show only moderate elevation of the basal metabolic rate. As a rule, thyroidectomy for diffuse toxic goiter is followed by satisfactory regression of exophthalmos; in some cases, however, exophthalmos will increase in degree after thyroidectomy or will even appear after operation although not present beforehand. The probable explanation of these findings is that the thyrotropic hormone of the anterior pituitary is directly responsible for the production of exophthalmos as well as for the stimulation of the thyroid parenchymal cells. Thyrotoxicosis is consequently an effect of Graves' disease rather than the cause. A balanced relationship<sup>3</sup> appears to exist between the pituitary gland and the thyroid, the pituitary thyrotropic hormone stimulating production of thyroxine and the increased quantity of circulating thyroxine tending to restrain further secretion of thyrotropic hormone. In addition, the parenchymal cells of the thyroid gland appear to inactivate the thyrotropic hormone present in the circulating blood.

Thyroidectomy will produce a satisfactory result in the great majority of patients with toxic diffuse goiter by interrupting the cycle of hormonal imbalance. In an occasional case of malignant exophthalmos with a minor degree of thyrotoxicosis, however, it is likely that the thyroid parenchyma for some reason neither is greatly stimulated by the thyrotropic hormone nor is able to inactivate it adequately. In these cases the specific effects of the excess thyrotropic hormone (for example, exophthalmos) are not relieved by thyroidectomy and may become even more pronounced after operation because of the removal of the restraining influence of thyroxine on the overactive pituitary gland. The suggestion has been made that postoperative thyroid crisis in Graves' disease may be due at least in part to the effects of the excessive thyrotropic hormone present in the circulating blood following excision of the thyroid. For this reason, some surgeons advocate the administration of desiccated thyroid or of thyroxine immediately following thyroidectomy for diffuse toxic goiter.

There are other indications that the pituitary thyrotropic hormone exerts a physiologically regulatory effect on thyroid

secretion. Administration of drugs which interfere with synthesis of thyroxine (thiourea derivatives) will produce a drop in basal metabolic rate proportionate to the decrease in synthesis of thyroid hormone. The thyroid gland in these cases, however, does not show decreased activity but actually shows hyperplastic parenchymal changes<sup>4</sup> strongly resembling those characteristic of toxic diffuse goiter. These histologic changes in the thyroid can be produced in normal experimental animals by administration of thiourea compounds but cannot be produced by these drugs if the pituitary gland has been previously removed. It is probable that as the drug decreases the discharge of thyroxine into the circulating blood, the hormonal balance between the pituitary gland and the thyroid becomes disturbed, with corresponding increase in secretion of thyrotropic hormone and consequent thyroid hypertrophy and hyperplasia.

### Physiologic Effects of Hyperthyroidism

Hyperthyroidism is characterized essentially by an excessively heightened metabolic rate, often increased as much as 50 to 100 per cent above normal, which affects all the tissues and cells of the body. As a result of the increased physiologic activity, a greater intake of food and fluids is required. If the hyperthyroidism is of mild degree, and if sufficient caloric intake can be maintained to keep pace with the increased metabolic requirement, no serious physical effects may result, although the patient may become moderately nervous and emotionally unstable. When physiologic activity is greatly heightened, on the other hand, the food intake cannot meet the energy requirements, wasting and breakdown of the body tissues occur, reserves of glycogen and of stored fat are depleted, and all the symptoms of sympathetic and central nervous system overstimulation become accentuated. Under these circumstances any coincidental organic disease that may be present will progress rapidly in extent and severity not only because of the added strain due to the generally increased body metabolism, but also because of the increased physiologic activity of the cells of the diseased organ or system itself.

In some cases overproduction of hormone is so marked that an actual state of intoxication (thyrotoxicosis) is produced.

Vomiting and diarrhea frequently appear and may not only interfere with the intake of greatly needed food and fluid, but also may contribute to their loss. Such patients exhibit a rapidly rising pulse rate and temperature, and within a short time the progressive picture in some cases may be completed by delirium, hyperthermia, extreme tachycardia, liver failure, and death in crisis.

As a result of the persistently increased total metabolism, there is a steady drain upon the physiologic reserves and an added load upon every organ and system of the body. The resultant effect upon the general health of the patient depends upon the degree of hyperthyroidism, the duration of the disease, the age of the individual, and the presence of concomitant visceral disease. The severity of hyperthyroidism alone may be of less importance than the presence of coincidental organic damage elsewhere in the body. Systemic disease of almost any type is markedly accentuated by hyperthyroidism even of mild degree, particularly if the thyroid overactivity is of long duration, since the damaged organs are forced to work constantly at an excessive rate. A young patient, organically sound, with diffuse toxic goiter of severe degree may be transformed into a satisfactory operative risk by a short period of proper preparatory treatment. On the other hand, a middle-aged subject with a mildly toxic goiter of many years' duration and with mild organic heart disease may be a dangerous risk because of the decreased cardiac reserve consequent to the prolonged overstimulation, even though the hyperthyroidism itself may be clinically mild.

Because the deterioration of organic physiologic reserves is so great, and because preoperative improvement in response to proper therapy is so prompt, the patient's physical condition and the extent of his ability to withstand operation should be estimated at the time of admission and before treatment of any kind has been instituted. An accurate evaluation of the degree of damage caused by the burning up of body tissues as a result of hyperthyroidism can be made best at this time and a tentative plan of management decided upon.

### Preoperative Preparation

The closest possible attention must be paid to the care of the thyrotoxic patient during the period preceding operation and during early convalescence. In few other diseases do minute and unremitting care together with accurate clinical judgment play such an important part in the successful management of an ill patient. Thyrotoxic individuals are usually excessively alert mentally as well as overstimulated physically and are easily tired, excited, or frightened. The utmost attention should be paid therefore to the elimination of possible annoyances. Investigation of the history and physical status, although necessarily detailed, may be spread over a period of several days rather than completed at one protracted and possibly exhausting visit. In like manner, laboratory examinations, roentgenograms, and basal metabolic rate determinations should never be allowed to overtax the endurance of a severely ill hyperthyroid patient. The procedure involved in the performance of each laboratory test, such as laryngoscopic examination or determination of the basal metabolic rate, should be explained to the subject's satisfaction if curiosity or concern is expressed, although the diagnostic implications involved, of course, are not discussed. Particular attention and consideration should be shown to patients who do not speak English well. The inability of these individuals to express their wishes and voice their fears and to receive satisfactory reassurance is a genuine handicap, and marked reduction of nervousness may follow a conversation by means of an interpreter. Every effort is made to shield the patient in these ways from any source of mental excitation or physical overexertion, since slight annoyances may rapidly increase the toxic manifestations of the disease and even such a minor procedure as the securing of a roentgenogram may initiate a crisis in some cases.

**Physical Examination.**—A complete physical examination is performed within a day or two after admission unless the thyrotoxicosis is of too severe a degree. The patient is weighed and the approximate amount of weight loss determined by questioning and by clinical estimation. These data are recorded, and a weight curve is plotted by determining the patient's weight every second day, preferably just before breakfast. The cardio-

vascular system is investigated with particular thoroughness; an electrocardiogram is made, and the degree of exercise tolerance is estimated. The pulse rate is noted on admission and is observed closely during the preoperative period. A roentgenogram of the chest is taken, both for evidence of parenchymal pulmonary disease and for evidence of possible displacement of the trachea or possible mediastinal extension of the goiter. Examination of the blood, in addition to the usual hemoglobin estimation and red cell and white cell counts, may include a cholesterol determination as well as a calcium determination for comparison with later findings in case symptoms suggestive of parathyroid deficiency develop after operation. The basal metabolic rate is estimated on two or three successive mornings, preferably in the patient's own room, to secure as accurate an initial reading as possible. Routine laryngoscopic examination is advisable before operation in all cases of thyroid disease. Involvement of a recurrent laryngeal nerve by a thyroid tumor may otherwise be mistaken for surgical injury if the lesion is not discovered until after operation. Finally, the liver function is estimated by means of appropriate tests, of which the Quick hippuric acid excretion test is probably the most satisfactory (p. 699).

**Primary Needs.**—The primary needs of the toxic thyrid patient are for rest, replacement of depleted physiologic reserves, and relief of toxicity. In thyrocardiac patients support of the damaged heart may be necessary also.

1. **REST.**—The patient is placed in a dark, quiet, private room, and the number of visitors is kept at an absolute minimum. Proper ventilation is secured, and the atmosphere should be kept cool, especially in the summer, although drafts must be avoided, since hyperthyroidism usually causes excessive sweating. Little exercise should be permitted because of the marked physiologic overactivity even while the patient is at rest. However, since prolonged rest in bed is likely to cause muscular weakness, the moderately thyrotoxic individual may be allowed up, in a wheel chair if necessary, for an hour or two each morning and afternoon. The nervousness and excitability characteristic of these patients can be controlled by phenobarbital or a shorter-acting barbiturate such as Nembutal in doses of 0.03 to 0.1 Gm. (gr.  $\frac{1}{2}$

to 1½) two or three times a day. Bromides, if preferred, are employed in doses of 0.6 Gm. (gr. 10) two or three times daily. Barbiturates are likely to produce excitation in some patients, and bromides sometimes cause mental confusion; in such cases, other sedatives are substituted. In the presence of marked thyrotoxicosis and impending crisis, mild sedatives may be entirely ineffective and the use of morphine in fairly large doses occasionally becomes necessary.

2. RESTORATION OF PHYSIOLOGIC RESERVES.--Autodestruction of body tissues as a result of the constant metabolic overactivity often causes extreme losses in body weight and in tissue and plasma proteins and may produce dehydration, depletion of liver glycogen, and vitamin deficiency states. For these reasons diet should be simple and easily digestible, high in caloric value (3,500 to 6,000 calories daily), high in vitamin content, and high in carbohydrate. While it is true that dietary protein exerts a high specific dynamic action and increases the output of body heat, it is also true that depleted protein reserves must be replaced. Addition of simple, easily digested proteins to the diet is advisable; the protein content of the meals is kept high and, in some cases, the use of intermediate nourishments made with skim milk powder or similar protein food is worth while. Since prolonged thyrotoxicosis may cause calcium depletion, the patient should take at least one quart of milk daily.

Frazier and Ravdin<sup>5</sup> suggest the use of vitamin B<sub>1</sub> (thiamine chloride) in full therapeutic doses, since this vitamin is concerned in the intermediary metabolism of carbohydrates and also since it is not stored in appreciable amounts. It is suggested that, since the clinical manifestations of vitamin B<sub>1</sub> deficiency are similar in some respects to the symptoms ordinarily noted in thyrotoxicosis, the occasional anorexia and the frequent cardiovascular symptoms seen in hyperthyroidism may be accentuated by avitaminosis B<sub>1</sub>. Therapeutic doses of the vitamin B complex are preferable to thiamine chloride alone.

Fluids are pushed, the patient being urged to take at least 4,000 c.c. daily. If this quantity is too great to be administered orally, infusions are given. All thyrotoxic patients must receive sufficient fluids to replace the abnormally large amounts lost; enough fluids are given to insure a daily urinary output of 1,000 to 1,500 cubic centimeters.

Severely ill patients, particularly those who exhibit nausea and vomiting, sometimes are not able to take any fluids and only a little food by mouth. These patients are best treated by administration of infusions of normal salt solution, protein hydrolysate solution, or dextrose (5 per cent) solution to maintain the proper daily total fluid intake. Not over 1,000 to 1,500 c.c. of normal salt solution is given in each twenty-four hours or salt retention may occur. Some commercial protein hydrolysate solutions contain significant amounts of sodium chloride; the amount of salt given in this way must be subtracted from the amount to be given as normal salt solution.

The plasma protein concentration should be determined at frequent intervals to detect the presence of hypoproteinemia, particularly after fluid balance has been restored. Anemia even of moderate degree in a thyrotoxic patient should be corrected by whole blood transfusions, since the increased oxygen requirements of the body tissues can be supplied only by a normal total volume of blood of normal oxygen-carrying capacity.

Determinations of liver function are repeated at intervals to note the progress of improvement in hepatic reserve. The administration of a high carbohydrate, high protein, high caloric diet and of large quantities of fluids is ordinarily sufficient to bring the hepatic function back toward normal. Additional measures for treatment of the liver damage often found in association with thyrotoxicosis are unnecessary.

### 3. RELIEF OF TOXICITY.—

*Thiouracil.*—Until recently the mainstay of the preoperative control of hyperthyroidism has been the use of iodine. An entirely new phase in the management of thyrotoxicosis, however, began with the demonstration by Astwood<sup>4</sup> that thiourea and its derivative thiouracil can be used safely to reduce the function of the hyperactive thyroid gland to a normal level. In the ensuing years thiouracil has been studied by internists as a method of treating hyperthyroidism medically, to enable the thyrotoxic patient to secure relief without recourse to operation, and by surgeons as a method of preparing seriously ill thyrotoxic patients for operation.

Administration of thiouracil, after a period of one or two weeks during which no effect may be noticed, causes a steady and



progressive reduction in basal metabolic rate, a decrease in signs and symptoms of toxicity, and a gain in weight. The patient shows uninterrupted clinical improvement and all evidences of hyperthyroidism disappear. The basal metabolic rate, in fact, can be depressed to a subnormal level by continued administration of full doses of thiouracil; the dose must be decreased as soon as the desired metabolic level is approached. As the thyrotoxicosis diminishes, the amount of iodine stored in the gland decreases and the level of blood iodine falls.

Histologically, however, the hyperplastic gland in treated thyrotoxicosis shows no evidence of involution such as is produced by the administration of iodine. Lahey and co-workers<sup>6</sup> have remarked that it is impossible to tell by microscopic examination of the thyroid gland whether a patient with toxic diffuse goiter received thiouracil before operation. Administration of thiouracil to a normal animal in the experimental laboratory will produce a fall in basal metabolic rate accompanied by marked hyperplastic changes and increased vascularity in the thyroid, with gross and microscopic evidence of the great hyperactivity characteristic of toxic diffuse goiter. Somewhat the same effects are noted in the thyrotoxic patient treated with thiouracil alone, the thyroid does not decrease in size but actually may become somewhat larger. At operation the gland is found to be brittle, friable, and extremely vascular, with every evidence of cellular hyperplasia and increased activity.

Thiouracil is believed to block normal synthesis of thyroxine in the thyroid gland by interfering with utilization of iodine. Because the output of thyroid hormone is decreased, the stimulating effect of the anterior pituitary thyrotropic hormone becomes proportionately more active. Increased vascularity and active hyperplasia develop in the thyroid as a result, although the heightened activity of the parenchymal cells is still insufficient to overcome the thiouracil block. The patient consequently is relieved of his symptoms but not of his disease, hyperplasia continuing in the thyroid although the basal metabolic rate drops to a normal level or even below. Since thiouracil interferes with synthesis of thyroxine, it is effective in both toxic diffuse and toxic nodular goiter, although response in the latter type is usually slow.

Effects of thiouracil continue as long as it is administered, withdrawal being followed after a short time by a gradual return to the previous state. Although use of thiouracil over a period of six to twelve months in patients with mild thyrotoxicosis is often followed by permanent disappearance of the disease, relapses will occur in almost half the patients after discontinuance of the drug; it cannot be depended upon to effect a cure.

The only apparently serious disadvantage of the use of thiouracil is its tendency to produce toxic effects. Approximately 13 per cent of all patients who take the drug will develop toxic reactions; about 60 per cent of these reactions will be serious enough to necessitate discontinuance of therapy. Of the patients treated with thiouracil, therefore, one in eight will develop toxic effects and one in twelve will be unable to continue use of the drug.

Significant *toxic reactions* attributable to thiouracil include agranulocytosis, leucopenia, drug fever, and dermatitis. Of these, agranulocytic angina is the most dangerous; all of the deaths that have been reported to follow use of thiouracil have been due to this complication. Appearing usually within the first four weeks of treatment and almost always within the first eight weeks, agranulocytosis is characterized by a sudden drop in total leucocyte count to levels below 4,000, with most marked reduction in the polymorphonuclear granulocytes. The earliest recognizable symptoms consist of sore throat, increasing fever, malaise, and finally prostration, with death resulting from ordinarily insignificant infections which the agranulocytic patient is unable to combat. Agranulocytosis represents more than one-fifth of all the toxic reactions caused by thiouracil and occurs in 2.5 per cent of all patients who take the drug. In a large series<sup>7</sup> of collected reports (5,745 patients), 14 per cent of the patients who developed agranulocytosis died, a total mortality of 0.4 per cent attributable to the use of thiouracil. The occurrence of agranulocytosis is not related to the dosage of the drug; it is necessary therefore for the physician to follow the patient's condition carefully, making total and differential leucocyte counts at least every seven to ten days and warning the patient to report immediately the occurrence of even a mild attack of sore throat, pharyngitis, or malaise. Treatment of agranulocytosis when it develops consists of immediate withdrawal of thiouracil, adminis-

tration of large doses of penicillin (50,000 units intramuscularly every two hours), and hospitalization of the patient. Other drugs such as pentnucleotides, yellow bone marrow concentrate (p. 280), crude liver extract, pyridoxine, and folic acid are not of proved effectiveness but may be given.

Leucopenia occurs in slightly more than 4 per cent of patients treated with thiouracil, appearing from the fourth to eighth week of therapy as a rule. The condition is asymptomatic, being characterized solely by a fall in leucocyte count to a level below 4,000, the differential count remaining relatively normal. Although not dangerous in itself, leucopenia may progress to agranulocytic angina at any time. A significant fall in leucocyte count occurring in a patient receiving thiouracil therapy therefore is an indication for immediate withdrawal of the drug.

Drug fever occurs in nearly 3 per cent of patients receiving thiouracil and may be accompanied by myalgic pains in the upper back and neck. It is important to differentiate drug fever, which is not directly dangerous, from fever due to infection complicating agranulocytic angina. Toxic dermatitis due to thiouracil therapy may be of various types, including urticaria and morbilliform or maculopapular eruptions. Drug dermatitis is a true toxic effect and drug fever is probably a sensitization phenomenon. Although these conditions are not dangerous in themselves, occurrence of either of them indicates an untoward reaction to thiouracil, administration of which should be stopped to avoid the possibility of more serious toxic effects.

Because of the high incidence of toxic reactions (13 per cent) and the fact that thiouracil treatment alone will produce as high a mortality rate (0.4 per cent) as surgery for moderately toxic goiter,<sup>8</sup> the general opinion is that this drug is not safe as a routine substitute for thyroidectomy in treatment of thyrotoxicosis. It is best used<sup>7</sup> only for preoperative preparation of poor-risk thyrotoxic patients or for treatment of thyrotoxic patients in whom operation is contraindicated. Thiouracil is not used when the risk of operation is small; for example, in patients with mild to moderate toxic diffuse goiter or in children with thyrotoxicosis. In such cases iodine alone is more rapid and safe and is equally effective.

Thiouracil is of most value in preoperative preparation of patients with severe degrees of thyrotoxicosis, heart disease

(thyrocardiac), marked weight loss, systemic disease involving other organs, or decreased resistance due to old age or prolonged illness. It is of value also when the use of iodine is contraindicated, as in patients with pulmonary tuberculosis or late syphilitic lesions. Other factors which in the past have contributed to the high surgical mortality in advanced thyrotoxicosis include the short period of time available for preparation when iodine is used alone (p. 738), the frequent lack of response to iodine (especially in toxic nodular goiter), and the distressingly high incidence of postoperative thyroid crisis in the most severely toxic patients. Thiouracil, which is effective in both toxic diffuse and toxic nodular goiter, has made it possible for the surgeon to spend as much time as he wishes before operation to restore the patient's weight and depleted physiologic reserves to normal, to operate upon a patient who is completely nontoxic, and to minimize the possibility of postoperative toxic reactions. When thiouracil is used in poor-risk patients, the mortality due to toxic drug reactions is insignificant in comparison with the consequent improvement in surgical mortality. When used in good-risk patients with mild or moderate degrees of toxicity, however, thiouracil does not reduce the surgical mortality but adds the possibility of toxic reactions from the drug. From a medical standpoint, thiouracil is of considerable value in treatment of thyrotoxic patients not suitable for operation; for example, in those with recurrent thyrotoxicosis with small remnants of gland remaining or in those with minor degrees of toxicity not severe enough to warrant thyroidectomy.

Divided doses of thiouracil are preferable to single daily doses; the drug is given in amounts of 0.1 Gm. every four hours or 0.2 Gm. three times daily until the basal metabolic rate has reached a nearly normal level. The antithyroid effect will continue for a week or more after discontinuance of thiouracil, so that continued administration of full doses will produce actual hypothyroidism. Lahey and co-workers<sup>4</sup> have stated that preparation requires in general a little more than one day for each 1 per cent the metabolic rate is elevated above normal; in most cases, full remission requires six to eight weeks of treatment. The increased vascularity and hyperplasia which occur in the thyroid gland following administration of thiouracil add greatly to the technical difficulties of thyroidectomy, to such an extent,

in fact, as almost to outweigh the advantages gained by use of the drug. This disadvantage can be overcome by the use of iodine during the last three weeks<sup>6</sup> before operation, administered together with thiouracil for two weeks and alone for the last week of preparation. Involution of the thyroid gland will occur satisfactorily under this plan, which combines the therapeutic advantages of both drugs. Thiouracil is omitted during the last week of preoperative preparation both because its antithyroid effect continues for a week or more after withdrawal and because toxic reactions may occur even after withdrawal. Iodine is continued in full dosage to the day of operation.

Because the period of preparation is so long, most patients may be treated on an ambulatory basis, hospitalization being required for clinical tests and general examination at the beginning of thiouracil treatment and again for final study during the last four or five days of preparation. Total and differential leucocyte counts are made at intervals of seven to ten days during treatment and the patient is warned to watch for symptoms suggestive of toxic effects, especially of agranulocytic angina. Use of thiouracil should not be discontinued if therapeutic response is slow; several weeks may pass before an effect is noted, particularly if the patient has received iodine in the past. Several months may be required for full effect.

Further search has been made for antithyroid drugs with the clinical effectiveness of thiouracil but without its toxicity. Astwood and associates, who have investigated many hundreds of such compounds experimentally in animals, have reported<sup>10</sup> the clinical use of *propylthiouracil* in one hundred consecutive patients with hyperthyroidism of all types and degrees. He states that propylthiouracil is a safe and effective antithyroid drug; not a single significant toxic reaction occurred in his reported group of cases. Others<sup>11,12</sup> have found that this drug, like thiouracil, will occasionally produce leucopenia and even agranulocytosis, however. On the basis both of the reports just mentioned and of those published by other investigators, propylthiouracil in general appears to be fully as effective as thiouracil and much less toxic.

Lahey and Bartels<sup>9</sup> advise the use of iodine together with propylthiouracil from the first day of treatment in patients with primary hyperthyroidism, severe hyperthyroidism with heart

failure, or thyroid crisis, since such patients may grow worse during the first week of treatment on propylthiouracil alone. Iodine will slow the response to propylthiouracil but will produce a more prompt relief of toxic symptoms; the basal metabolic rate on this plan of treatment will drop to normal at a rate of approximately 1 per cent daily. As in the case of other thiourea drugs, propylthiouracil is discontinued a week before operation, while iodine is continued to the day of operation. These authors feel that because of the equal effectiveness and low incidence of complications with propylthiouracil (2 per cent), this drug should replace thiouracil for preoperative preparation of thyrotoxic patients. The dose of propylthiouracil suggested is 200 mg. daily (100 mg. every twelve hours). When propylthiouracil is used, total and differential leucocyte counts should be made at regular intervals to anticipate the possibility of leucopenia or agranulocytic angina. There are apparently no contraindications to use of the drug in children, in diabetic patients, or in pregnant women.

*Iodine.*—While thiouracil and propylthiouracil appear to be superior to iodine for reduction of the elevated basal metabolic rate to normal, iodine still plays an essential part in preparation for thyroidectomy. The thiourea drugs alone will cause increased vascularity and hyperplasia of the thyroid to such an extent that surgical removal becomes technically difficult. If iodine also is administered during at least the last three weeks of preoperative preparation and thiouracil (or propylthiouracil) is discontinued a week before operation, the advantages of both drugs are obtained, relief of toxicity being followed by satisfactory involution. Iodine alone is used in preparation of children and of patients with milder degrees of toxic diffuse goiter, particularly if the symptoms are of short duration. Thiouracil induces serious toxic reactions in a high percentage of patients (8 per cent), and propylthiouracil also may cause toxic effects; iodine must be used alone in these occasional cases also.

The soft, highly vascular, overactive, hyperplastic gland typical of toxic diffuse goiter contains little colloid secretion and has an iodine content well below the normal level, although the blood iodine is considerably elevated during the first few months of the disease. With the continued drain upon the body iodine reserves by the hyperfunctioning thyroid, the blood iodine later

begins to drop until the total iodine stores of the body become depleted, and, within a year or more following the onset of illness, both gland and blood iodine concentrations fall below the normal level.

Therapeutic administration of iodine produces a rapid and sweeping change. Involution of the thyroid gland takes place within a few days, colloid accumulates in the acini, the iodine content of the gland rises rapidly to a value well above normal, the blood iodine level rises, and characteristic systemic effects are noted. The nervous manifestations decrease and may almost disappear, the pulse rate falls steadily toward normal, the elevated basal metabolic rate shows a marked and progressive drop, and the patient feels greatly improved and begins to gain weight rapidly. This series of changes in response to iodine medication takes place in approximately 90 per cent of thyrotoxic patients. Such improvement can almost always be attained in patients with toxic diffuse goiter (exophthalmic goiter), but patients with toxic nodular goiter are much less responsive to iodine medication. However, iodine does no harm and therefore should be given as a preoperative preparatory measure to every thyrotoxic patient, whether or not thiouracil is used, even though the gland is of the nodular type, since it is impossible to determine whether a particular gland will be favorably affected by iodine therapy.

Within ten to twenty days the clinical improvement in response to iodine reaches its maximum and remains at a plateau for several days. Then, as the gland adapts itself to the colloid distention,<sup>6</sup> the optimum level of improvement is no longer sustained and clinical regression sets in, with the progressive return of toxic symptoms. After the remission has passed and toxic manifestations have reappeared, the patient is relatively iodine fast, and an equally high peak of improvement cannot be reached by further administration of iodine, although considerable improvement may be maintained. Certain well-recognized authorities believe that the existence of iodine fastness and iodine escape is doubtful, but it is nevertheless true in general that the beneficial effects of iodine decrease steadily and rapidly after the maximum clinical improvement has been reached and maintained for several days. It is of the greatest importance for the surgeon to realize that clinical improvement in thyrotoxicosis following iodine therapy is temporary in nature.

Iodine is best given in the form of Lugol's solution in grape juice or milk as a vehicle, 10 to 15 minims being administered after each meal and at 8:00 P.M. The usual dose amounts to 40 to 50 minims each day. If the patient is unable to take the medication by mouth, it may be added to an infusion and administered intravenously or by hypodermoclysis in normal salt solution. Diiodotyrosine, although closely related to thyroxine, is relatively inert; sodium iodide, too, is somewhat less satisfactory in its effect than is Lugol's solution.

A report has appeared<sup>11</sup> detailing the apparently successful treatment of a patient with metastatic adenocarcinoma of the thyroid by means of *radioactive iodine* administered orally, clinical and roentgenographic evidence all indicating arrest if not regression of the metastatic tumor areas. An interesting new field of therapy is being developed in the use of radioactive isotopes, which substitute effective internal irradiation for external irradiation. Although definite untoward effects and contraindications have been noted, the use of radioactive substances administered orally appears to hold definite promise as a mode of specific radiation therapy in certain diseases.

### Associated Heart Disease; Thyrocardiac Patients

The primary effect of hyperthyroidism upon the cardiovascular system is the production of tachycardia, both because of the direct action of the thyroid secretion upon the heart cells themselves and because of the increased metabolic activity of the entire body. Toxic goiter, even if severe and of prolonged duration, will produce no characteristic pathologic change in the myocardium of a heart undamaged by any other lesion.

The cardiac reserve is essentially the difference between the greatest activity of which the heart is capable without failing and the basal level at which it works in the absence of any stress. Thyrotoxicosis, by means of constant stimulation to overactivity, elevates the basal level of cardiac function toward the upper limit of capacity in proportion to the degree of thyrotoxicosis and consequently decreases the reserve. Even when the thyroid hypersecretion is of severe degree and of protracted duration, the reserve of the normal heart undamaged by associated unrelated disease usually is sufficient to prevent failure. As many au-



thorities have pointed out, however, patients with advanced degrees of diffuse toxic goiter occasionally may develop cardiac failure as a result of the prolonged and extreme tachycardia alone. If the toxic goiter is removed in such a case, the heart will return to normal with no residual damage resulting from the thyroid disease.

In general, cardiac decompensation in association with hyperthyroidism results from the effect of the excess thyroid secretion upon a previously damaged heart. Persistent hyperthyroid tachycardia, for example, in a middle-aged individual with sclerotic changes in the cardiovascular system or with a cardiac valvular lesion will produce a marked accentuation of the otherwise subclinical cardiovascular changes. The cardiac reserve in such a patient is decreased both by a lowering of the upper limit of functional capacity and by an elevation of the basal level of activity. Auricular fibrillation and cardiac failure may develop following prolonged or severe thyrotoxic stimulation of the slightly damaged heart with a moderately diminished reserve. Many such patients are treated for heart disease alone, the contributory effect of hyperthyroidism remaining unrecognized. Thomas<sup>12</sup> states: "The fact that a nodular goiter may exist for a long time before cardiac symptoms develop has led some people to believe that nodular goiter may damage the heart. We have seen no proof of this and are inclined rather to believe that a mild degree of hyperthyroidism which has existed for some years finally becomes evident when the cardiac reserve has been diminished." In cases of this type the cardiac damage may progress to actual functional failure with few outstanding evidences of the hyperthyroidism which has been imposing an insupportable load upon a weakened heart. Lahey<sup>13</sup> suggests that every decompensated cardiac patient who does not respond satisfactorily to proper supportive therapy, particularly in the presence of auricular fibrillation, should be investigated for possible associated hyperthyroidism.

Although the methods of distinguishing between congestive cardiac failure with and without the presence of contributory hyperthyroidism are not within the province of this work, it may be stated that thyrocardiac disease is usually accompanied by a loss in weight typical of latent hyperthyroidism but unexplainable on any other basis, a consistent elevation of pulse rate that

cannot be reduced effectively by bed rest and digitalization, a history of impaired cardiac function over a very long period, a consistently elevated basal metabolic rate, and a discrepancy between the degree of discoverable cardiac damage and the degree of failure.

Since hyperthyroidism occurring in patients with unrelated heart disease accentuates the cardiac disability, operation is strongly indicated, even in the presence of decompensation. Removal of the added load imposed by thyroid overactivity will often rapidly restore cardiac capacity to an amazing degree, and the operative risk is not especially great even if cardiac failure is present at the time of admission, provided that proper preparatory measures are instituted.

Preparation of these patients for thyroidectomy will require six to ten weeks of thiouracil (propylthiouracil) therapy, during which time measures are taken also to improve the cardiac status. Early congestive heart failure is managed in the usual way, by institution of bed rest, adequate sedation, and restriction of salt intake. All evidences of cardiac failure will disappear in most cases when the basal metabolic rate has reached normal in response to thiouracil and iodine, and operation then may be undertaken without further delay. When thiouracil produces a toxic reaction, iodine must be used alone; in these patients, response to preoperative therapy is much more prompt but much less complete. Thyroidectomy can be done in a single stage in patients prepared with thiouracil and iodine; two-stage operations often are necessary in severely toxic thyrocardiac patients prepared with iodine alone.

Patients with cardiac decompensation of advanced degree who do not improve after bed rest and antithyroid therapy are treated by the administration of digitalis in full doses, particularly if auricular fibrillation is present. Diuretics, such as Salyr-gan (1.0 c.c. hypodermically), are useful in relieving cardiac edema in some cases. It is not advisable to attempt to restore normal cardiac rhythm in a thyrotoxic patient with auricular fibrillation by the use of quinidine before operation, since quinidine, always potentially toxic, is even more likely to produce an untoward reaction in a hyperthyroid patient. Moreover, as pointed out by Thomas,<sup>12</sup> a fibrillating heart in the presence of thyrotoxicosis can be controlled more effectively by digitalis

than can a failing heart with normal rhythm. If normal rhythm is restored by means of quinidine to a fully digitalized fibrillating heart, effect of the digitalis may be lost with the reversion to normal rhythm, and the pulse rate may rise to an exceedingly high level, decreasing the circulatory efficiency. Finally, even though normal rhythm sometimes will be restored by the use of quinidine during the preoperative period, the added cardiac strain immediately following operation may again precipitate fibrillation at the very time when cardiac failure is most dangerous. In many such cases, reversion to normal rhythm will occur spontaneously after removal of a toxic thyroid, and in practically every case of thyrocardiac disease the degree of cardiac failure will be greatly reduced by thyroidectomy.

### Thyroid Crisis

Thyroid crisis has been practically eliminated as a postoperative complication in patients prepared with thiouracil. Such patients, even if toxicity is severe, can be relieved completely of hyperthyroidism and brought to a normal metabolic state if thiouracil can be given for the proper length of time and in the proper dosage before operation. Because of its equal effectiveness and lower toxicity, it is probable that propylthiouracil will prove even more useful than thiouracil. Since the thiourea drugs require several days to initiate their effect, iodine is given also from the first day of treatment in severely toxic patients. There is little doubt that proper use of this combination of drugs will go a long way toward eliminating crisis as a cause of mortality in thyrotoxicosis if treatment can be begun before onset of the thyroid storm.

The possibility of thyroid crisis can be anticipated in patients with severe toxicity, extreme loss of weight and nutritional depletion, serious complicating disease, and insufficient response to treatment. Danger signs during the preoperative period include a steady and continued rise in pulse rate, basal metabolic rate, and general metabolic activity, an increase in the severity of psychic disturbances, and a failure to gain weight on an adequate caloric intake. In these patients, autodestruction of body tissues in response to the excess thyroid secretion is accelerated beyond the point of physiologic compensation, and profound intoxica-

tion develops. The progression of severe thyrotoxicosis into thyroid crisis is indicated by the appearance of protracted insomnia, gastrointestinal upsets with nausea, vomiting, and diarrhea, increasing hyperthermia with a temperature elevation sometimes as high as 105 or 106° F., extreme tachycardia with generalized flushing of the skin and profuse sweating, and, finally, toxic delirium, coma, and death. It is probable that liver failure plays an important part in the development of thyroid crisis; jaundice is occasionally observed.

A crisis may be brought on in severely ill hyperthyroid subjects even by minor laboratory procedures or examinations. If toxicity is marked, the patient should be allowed complete rest. Not even a basal metabolic rate determination should be performed or a roentgenogram taken until the general condition has shown marked improvement in response to treatment.<sup>14</sup>

Fully developed thyrotoxic crisis is an acute medical emergency, carrying the threat of imminent death; the mortality rate in one relatively large series is reported as 67 per cent.<sup>15</sup> The patient must be placed in a private room with a special nurse constantly in attendance and all sources of disturbance eliminated. Complete rest is of the utmost necessity. Morphine or some equally powerful narcotic is given frequently and in relatively large doses until the patient is asleep or until the respiratory rate is depressed as low as 15 per minute. The hyperthermia is reduced by surrounding the patient with well-wrapped ice bags, and a small, well-protected ice bag is placed upon the precordium. Alcohol sponges are given at intervals. Since the oxygen requirements of the body may be almost doubled by the heightened metabolic rate, the patient should be placed in a standard oxygen tent, or a nasal oxygen catheter should be inserted, regulated to supply 50 to 60 per cent oxygen.

Dehydration is combated by the administration of fluids intravenously, preferably by continuous drip. A minimum of 1,000 c.c. of normal salt solution and 3,000 c.c. of dextrose (5 to 10 per cent) solution is given daily by infusion, and carbohydrates are supplied by mouth if the patient is able to swallow. Continuous administration of large quantities of carbohydrate is necessary to increase the hepatic reserve, to supply fuel for the heightened metabolism, and to prevent the development of acidosis. Lugol's solution is added to the intravenous fluids in divided

doses in sufficient quantity to total 50 minims daily. Administration of the medication by mouth is not entirely satisfactory, since vomiting often occurs. The use of iodine in this manner is of the greatest importance in reducing the activity of the thyroid gland. Thiouracil and propylthiouracil will restrain further activity of the thyroid but will produce little visible effect until the stored and circulating thyroid secretions drop to less dangerous levels. Because of their delayed effect, the thiourea drugs are of no value in the treatment of actual or impending thyroid crisis.

Large doses of the B complex vitamins and vitamin C are given, preferably intravenously together with the infusions.

When organic heart disease is associated with hyperthyroidism, signs of congestive failure will appear at the onset of a severe thyrotoxic state and indicate the necessity for rapid and full digitalization (p. 245), if this has not already been accomplished before the onset of crisis. Digitalis is not used in the treatment of thyroid crisis in the absence of definite signs of cardiac failure, however, since the extreme tachycardia characteristic of this thyrotoxic state is not an evidence of heart failure but is partly a direct result of the action of the thyroid secretion upon the heart cells themselves. Diminution of the cardiac output and decrease in the rate of a normal heart by the use of digitalis in the presence of thyroid crisis may depress the circulatory efficiency below the level required by the heightened physiologic activity of the body tissues.

After recovery from crisis the patient should be watched for two or three weeks, during which time the administration of large quantities of fluids, carbohydrates, and other nutritional factors should be continued and iodination maintained. Operation is ordinarily performed in two or more stages on patients of this type who have been severely ill.

### When to Operate

Selection of optimum time for operation upon the thyrotoxic patient is simple when thiouracil is used for preparation; thyroidectomy is performed when the basal metabolic rate has been reduced to normal (0 to +10) and all evidences of toxicity have disappeared. The decision of when to operate is more difficult, however, when thiouracil cannot be used and iodine must

be given alone; such cases have become rare since propylthiouracil has become available and the need for prolonged treatment is recognized. If iodine alone is used for preparation, however, the patient should have a competent cardiovascular system and should exhibit a recent gain in weight, decrease in resting pulse rate (below 100), decrease in basal metabolic rate (below 30), and definite decrease in toxicity and excitability and should be fully iodinated before operation is performed.

Operation is dangerous if the patient exhibits prolonged insomnia, rising pulse rate, continued weight loss, and increasing toxicity in spite of treatment. No surgical procedure is permissible if nausea, vomiting, diarrhea, or marked psychic irritability is present, since any of these manifestations may indicate an approaching thyrotoxic crisis.

The opinion has been held in the past that hyperthyroid patients should not be told of the date and time of operation to avoid producing excitement and a wakeful and restless night before operation. This precaution is no longer widely observed since more effective methods of reducing toxicity before operation have been introduced.

### Postoperative Care

The patient is placed flat on his back in bed after operation, with the head turned to one side to facilitate breathing and to permit emptying of the stomach if vomiting occurs. If the patient desires, Fowler's position may be assumed after recovery from anesthesia. Sudden overextension of the neck must be avoided, particularly while the patient is being returned from the operating room. A small pillow will afford comfort after consciousness returns. The patient may be allowed up a day or two after operation, if his condition permits.

Pain following thyroidectomy is usually not severe except upon swallowing, so that one or two doses of morphine will ordinarily be all that the patient will require after operation. Opiates should be used as sparingly as possible after thyroid surgery because of their tendency to depress respiration and therefore to encourage the development of pulmonary complications.

Fluid administration is continued, sufficient quantities of normal salt and dextrose (5 per cent) solutions being given intravenously to insure a daily urinary output of 1,000 to 1,500 c.c. as well as to supply sufficient carbohydrate to forestall the development of acidosis. The average patient is reluctant to swallow even water during the first two or three days, and reliance must be placed upon the parenteral administration of fluids, either by continuous or intermittent infusion. Oral feeding must be resumed as soon as possible. Transfusion of blood is occasionally necessary to combat anemia, but particular care must be taken in cross-matching and in administration of blood if the patient shows evidences of marked toxicity, since a slight transfusion reaction may be sufficient to precipitate a state of crisis.

Although it is probably of little or no value except when relatively large amounts of thyroid tissue are left behind, administration of iodine is continued without interruption following operation, especially if toxicity is severe. Administration by means of a retention enema is not dependable, since absorption from the rectum is variable in degree; the drug is best given either orally or intravenously. The medication is also given throughout the intervals between stage operations when iodine alone has been used, in order to maintain optimum iodination of the thyroid gland.

Oxygen should be given to severely toxic patients, both to avert the development of crisis and to support the overactive myocardium, especially if cardiac disease is present. The use of oxygen is an absolute necessity in the treatment of severe postoperative thyrotoxicosis. On the other hand, occasional deep respirations also must be encouraged, either by voluntary effort or by inhalation of carbon dioxide (5 per cent), since these patients are susceptible to the development of postoperative pulmonary atelectasis.

Dressings should not be applied so tightly to the wound that interference with movement or with respiration will occur; if the patient complains of discomfort, the bandage should be loosened at once. Voluminous or heavily padded or taped dressings are not necessary and may be a source of considerable annoyance. If a drain has been inserted at operation and left projecting from the incision, it should be withdrawn after

twenty-four hours. Alternate skin sutures or clips are removed forty-eight hours after operation, and the remainder on the following day. No difficulty is encountered because of the early removal of sutures and the resulting scar is less noticeable.

### Minor Complications

Dysphagia, or pain on swallowing, is moderately severe during the first two days but disappears rapidly after this time. The difficulty experienced in taking fluids can be minimized by having the patient use a straw and bend his head well forward to relax tension on the neck. Tracheitis is also an annoyance commonly experienced during the early postoperative period and is especially distressing when the patient is unable to make the efforts required to clear the throat of mucus. Tracheal irritation can be controlled by the administration of steam inhalations with added compound tincture of benzoin, either continuously or at three-hour intervals. Sometimes, too, the subject may be able to cough up the mucus if the bed is replaced in a horizontal position and the head is flexed on the chest. Because tracheitis with resultant mucoid exudation is so common, medications which have a tendency to depress the respirations and the cough reflex should be used sparingly.

### Major Complications

**Thyroid Storm or Crisis.**—Most fatal of all the untoward occurrences that may appear following removal of a toxic goiter is the development of a thyroid storm or crisis. There appears to be little danger of crisis occurring in patients adequately prepared with thiouracil; this antithyroid drug appears to have minimized crisis as a complication of toxic goiter. Thyroid crisis still may occur, however, in patients prepared with iodine because of inability to take thiouracil or, more commonly, in patients first seen in too advanced a stage of thyrotoxicosis to permit treatment with thiouracil, which acts so slowly. Although this condition sometimes appears without warning and through no fault of the surgeon, it is often a result of operation before the peak of improvement has been reached in response to pre-operative treatment or of excessive surgery on a severely ill patient. If a satisfactory response to thiouracil (or propyl-



thiouracil) does not occur as promptly as expected, administration of the drug in full dosage should be continued until the proper reduction of toxicity has finally been achieved; operation is definitely dangerous before a full response to antithyroid therapy has been attained.

Postoperative thyroid crisis appears within four hours to four days after operation and is characterized by rapidly increasing toxicity, steadily rising pulse rate and temperature, vomiting and diarrhea, and extreme excitation and hyperirritability, with the subsequent development of delirium, progressively deepening coma, and finally death.

Treatment of thyroid crisis is the same whether it develops before or after operation (p. 743). If cardiac failure is associated with thyrotoxic storm, full digitalization should be accomplished by a rapid method. Simple thyrotoxic tachycardia, however, must not be mistaken for cardiac failure, no matter how marked the acceleration of the pulse may be, since the use of digitalis is not advisable in the absence of signs of cardiac failure or auricular fibrillation.

**Respiratory Obstruction.**—Simple postoperative tracheitis will produce a temporary hoarseness which disappears within several days. Injury to a single recurrent laryngeal nerve at operation may produce a more prolonged alteration in voice quality, varying from a pronounced huskiness to no change whatever in voice quality or in respiration. In the latter case, permanent paralysis of one vocal cord may remain unsuspected and undiscovered unless routine laryngoscopic examination is performed before discharge of the patient.

**BILATERAL PARALYSIS OF THE INFERIOR LARYNGEAL NERVES.**—Although this condition is rare, it is an extremely unfortunate accident. The resulting symptoms vary in the early stages. Sudden complete obstruction to inspiration may occur during the operation itself unless intratracheal anesthesia is being used. In some cases respiratory difficulty does not appear at once but the patient is totally unable to speak when consciousness returns. Other patients will partially retain their ability to speak but will exhibit immediate and severe obstruction to respiration. The complication is of especial danger because it decreases the ability of the toxic patient to obtain the

increased amount of oxygen required by the heightened metabolic processes. Paralysis of both vocal cords necessitates immediate tracheotomy in most cases.

No further treatment is possible during the early post-operative period. Some patients who exhibit simple aphonia at this time, without respiratory obstruction, may notice no great difficulty in breathing, for several months but always develop an increasing inspiratory stridor after that time because of the progressive fibrotic narrowing of the paralyzed vocal cords.

If the accident is discovered during the operation, efforts should be made to locate and anastomose the divided ends of the nerves if the condition of the patient will permit the additional surgery, and a tracheotomy must be performed under all circumstances.

The tracheotomy is permanent and the tube usually must be worn throughout the duration of life. In many cases the patient is enabled to speak by closing the end of the tube temporarily with a finger. The only satisfactory alternative at present to the wearing of a permanent tracheotomy tube is the sub-mucous resection of a vocal cord, which permits the patient to breathe in a normal manner by permanent sacrifice of the voice, only a hoarse whisper being possible after the operation.

Surgical exposure and reanastomosis of the divided recurrent laryngeal nerves at a later date has been advised,<sup>16</sup> but the results of such an operation are far from satisfactory and the procedure is entirely useless if more than two or three months have passed since the original injury. King<sup>17</sup> has reported in detail an operation for restoring function in case of bilateral recurrent nerve paralysis. He claims successful restoration of both phonation and respiration in one of the three cases reported and less complete but still satisfactory results in the other two. The operation involves transplantation of the omohyoid muscle to the arytenoid cartilage, on either one or both sides in recently injured cases, together with laryngeal reconstruction in old cases. Modifications of this operation have been suggested,<sup>18 19</sup> with excellent clinical results reported.

**TRACHEAL COLLAPSE.**—Tracheal collapse may follow removal of a massive nodular goiter which has caused prolonged compression of the trachea. If evidence of tracheal deviation

or compression is visible on preoperative roentgenography, intratracheal anesthesia should be used to prevent collapse of the trachea during operation, and a tracheotomy is done after removal of the tube if necessary. Such an accident also sometimes follows removal of a malignant tumor of the thyroid.

**POSTOPERATIVE HEMORRHAGE.**—This complication, serious because of the danger of sudden and complete respiratory obstruction rather than because of blood loss, is most likely to occur within a few hours after operation. Significant hemorrhage into the field of operation usually arises from a large branch of the superior or inferior thyroid artery; the space beneath the prethyroid muscles fills rapidly with blood under considerable pressure. Moderate swelling of one or both sides of the neck is visible externally after the dressings are removed; the involved area is firm or even hard to the touch. Immediate release of the retained blood is a vitally necessary emergency measure to release tracheal compression and to prevent suffocation. The dressing should be removed promptly and the wound opened by introduction of a sterile clamp in the midline between the prethyroid muscles to allow escape of blood from the pretracheal compartment. There may be no time to wait for the surgeon to arrive; sudden extreme dyspnea appearing shortly after thyroidectomy is sufficient justification for the intern or resident to open the incision promptly on his own responsibility. Release of pressure relieves the dyspnea at once. A sterile dressing is applied and the patient is taken immediately to the operating room, where the bleeding vessel is found and ligated. If the bleeding point cannot be identified, the superior and inferior thyroid arteries are ligated on the side of the hemorrhage or on both sides if advisable.

Small hematomas or accumulations of serum under the skin flaps can be evacuated by puncture with a fine probe or needle at the time the first sutures are removed. Wide areas of induration occasionally appear, particularly when moderately heavy catgut has been used. Unless actual infection develops, these diffuse hematomas will disappear with little reaction if allowed to absorb spontaneously.

**Pulmonary complications** are unusually common after thyroidectomy in elderly people, especially if the goiter is of

long standing duration or if significant systemic disease is present. Depression of respiration or of the cough reflex by excessive sedation must be avoided, and if any evidence of tracheal or bronchial exudation of mucus appears, inhalations of medicated steam and administrations of carbon dioxide (5 per cent) are given at intervals. While the use of oxygen is indicated during the early postoperative period, particularly in patients in the upper age groups and in severely toxic subjects, the depressing effect of the gas on respiratory rate and amplitude must be kept in mind and the possible development of pulmonary atelectasis anticipated. Pneumonia also may occasionally appear following the milder postoperative thyrotoxic reactions in weakened subjects.

Wound infection is not commonly seen following thyroidectomy except after the removal of a large nodular goiter, with extensive dead space and widespread distortion of normal structures resulting. Treatment of this complication differs in no way from the management of infection developing in any wound. The occurrence is an unfortunate one, however, since the incisional scar is likely to be somewhat more fibrotic and more noticeable after recovery. It is of great importance to realize that the appearance of even a minor infection in a thyrotoxic patient may result in accentuation of the hyperthyroidism and may even precipitate crisis. Mediastinitis, a highly fatal complication, is very rare.

Parathyroid tetany has become an uncommon complication of thyroidectomy since the recent advances in operative technique have become more widely adopted and practiced. The parathyroid glands, because of their small size and variability in location, may easily be injured during the excision of a goiter by interference with their blood supply, by direct trauma, or by postoperative edema. Sometimes they may even be totally removed. Permanent parathyroid deficiency invariably follows complete extirpation of all parathyroid gland tissue. If one uninjured gland is left behind or if the parathyroid tissue is simply damaged during operation, the resulting tetany ordinarily will be less severe and will be temporary in nature, spontaneous recovery ensuing.

The onset of parathyroid tetany develops within two to five days after operation and is marked clinically by increasing irritability and involuntary twitchings of all the skeletal muscles, with a definite sensation of tightness in the face as a result of the hypertonicity of the facial musculature. Numbness and stiffness of the hands and feet also appear. At this point the patient becomes anxious and apprehensive because of the generalized hypertonus. Spasmodic muscular contractions can be elicited in various ways in these patients; a light tap over the region of the facial nerve will characteristically produce a twitching of the angle of the mouth on the same side (Chvostek's sign) and a slight blow over the peroneal nerve in the popliteal fossa will produce a sudden eversion of the foot. Occlusion of the blood supply to the hand by means of a sphygmomanometer within several minutes will bring about a typical paroxysm of tetany (Trousseau's sign), with powerful adduction of the thumb and flexion of the extended fingers at the metacarpophalangeal joints.

If the tetany is more severe, the muscles of the face and throat become tonically contracted and the patient has difficulty in speaking or swallowing. As the generalized muscular hypertonus becomes more marked, the hands and feet both develop the characteristic hypertonic spasm. The wrists and elbows are flexed and the legs extended, and the muscular hypertonicity may be so extreme that passive movement is resisted powerfully. Smooth muscles occasionally become affected, as evidenced by increased intestinal peristalsis. Tonic contractions of this type persist for several minutes or even for hours and are associated with cramping pains in the muscles.

Examination of the blood in parathyroid deficiency will reveal a decrease in calcium and an increase in phosphorus content although, as a rule, symptoms of tetany do not appear until the calcium level has dropped from the normal average value of 10 mg. per cent to a value below 7.5 mg. per cent. Decreased serum calcium in association with generalized muscular hypertonicity is diagnostic of parathyroid tetany.

Treatment of the condition is directed toward immediate elevation of the calcium content of the blood and substitution therapy for the parathyroid hormone deficiency. Calcium chloride (10 c.c. of 5 per cent solution) or calcium gluconate

(10 c.c. of 10 per cent solution) may be injected intravenously. The sterile solution, which should be introduced very slowly to avoid a reaction, often occasions a sensation of generalized warmth. If a satisfactory vein is not available, calcium gluconate solution may be given intramuscularly. To maintain the blood calcium at a fairly high level, calcium lactate or calcium gluconate should be given in solution at frequent intervals by mouth in amounts totaling 4 to 10 Gm. daily. The drug is best administered dissolved in water. Parathyroid hormone, of which several commercial preparations are available, may be given subcutaneously in doses up to 100 units a day. Not over one daily dose is required, and, since the drug tends to become less effective after continued use, it should be administered only in case of necessity. Frequent determinations of the serum calcium level are made to avoid hypercalcemia if parathyroid hormone is used regularly.

The best therapeutic agent available for correction of hypocalcemia due to parathyroid deficiency is dihydrotachysterol (A. T. 10), a derivative of irradiated ergosterol. The drug, as employed by McCullagh and Ryan,<sup>20</sup> is administered orally in capsules as a 0.5 per cent solution in oil of sesame, in doses varying with the degree of parathyroid deficiency. At the beginning of treatment, the initial daily dose may be as much as 2 c.c. administered in fractional dosage, the quantity being decreased as the serum calcium rises to a normal level of 9 to 10 mg. per cent. Like vitamin D, dihydrotachysterol exerts its effect by promoting absorption of calcium from the intestine; calcium lactate or calcium gluconate is administered in conjunction with A. T. 10 in total amounts of 5 to 10 Gm. daily in dilute aqueous solution. Permanent adjustment of the dose of dihydrotachysterol is achieved by repeated determinations of the serum calcium level during the course of therapy. The average patient will require from 0.5 to 0.75 c.c. of the drug every day or every other day, together with calcium in proper quantities, to maintain the blood calcium level within the normal range. Overdosage may cause hypercalcemia with characteristic toxic effects; dihydrotachysterol should not be used unless facilities are available for repeated determinations of blood calcium concentration.

Vitamin D therapy is used to treat infantile tetany; it is reported to be effective also in parathyroid tetany. Vitamin

D<sub>2</sub> (calciferol) appears to be particularly effective; like dihydrotachysterol, it promotes absorption of calcium from the intestine. The vitamin is given in doses of 100,000 units daily<sup>21</sup> together with calcium lactate or gluconate in amounts of 5 to 15 Gm. in aqueous solution. Close watch must be kept upon the serum calcium level to avoid hypercalcemia.

### References

1. Means, J. H.: The Nature of Graves' Disease With Special Reference to its Ophthalmic Component, *Am. J. M. Sc.* 207: 1, 1944.
2. Marine, D.: Studies on the Pathological Physiology of the Exophthalmos of Graves' Disease, *Ann. Int. Med.* 12: 433, 1938.
3. Salter, W. T.: The Endocrine Function of Iodine, Cambridge, Mass., 1940, Harvard University Press.
4. Astwood, E. B.: Treatment of Hyperthyroidism With Thiourea and Thiouracil, *J. A. M. A.* 122: 78, 1943.
5. Frazier, W. D., and Ravdin, I. S.: Use of Vitamin B<sub>1</sub> in the Preoperative Preparation of the Hyperthyroid Patient, *Surgery* 4: 680, 1938.
6. Lahey, F. J., Bartels, E. C., Warren, S., and Meissner, W. A.: Thiouracil—Its Use in the Preoperative Treatment of Severe Hyperthyroidism, *Surg., Gynec. & Obst.* 81: 425, 1945.
7. Van Winkle, W., Hardy, S. M., Hazel, G. R., Hines, D. C., Newcomer, H. S., Sharp, E. A., and Sisk, W. N.: The Clinical Toxicity of Thiouracil, A Survey of 5,745 Cases, *J. A. M. A.* 130: 343, 1946.
8. Fowler, E. F., and Cole, W. H.: The Advantages and Limitations of Thiouracil Therapy in Thyrotoxicosis, *Surg., Gynec. & Obst.* 81: 350, 1947.
9. Lahey, F. H., and Bartels, E. C.: The Use of Thiouracil, Thiobarbital, and Propylthiouracil in Patients With Hyperthyroidism, *Ann. Surg.* 125: 572, 1947.
10. Astwood, E. B., and Vanderlaan, W. P.: Treatment of Hyperthyroidism With Thiouracil, *Ann. Int. Med.* 25: 813, 1946.
11. Seidlin, S. M., Marinelli, L. D., and Oshry, B.: Radioactive Iodine Therapy, *J. A. M. A.* 132: 838, 1946.
12. Thomas, H. M., Jr.: Heart in Hyperthyroidism, *Ann. Int. Med.* 5: 184, 1931.
13. Lahey, F. H.: Hyperthyroidism Associated With Cardiac Disorders, *Surg., Gynec. & Obst.* 50: 139, 1930.
14. Bayley, R. H.: Thyroid Crisis, *Surg., Gynec. & Obst.* 59: 41, 1934.
15. McArthur, J. W., Rawson, R. W., Means, J. H., and Cope, O.: Thyrotoxic Crisis, *J. A. M. A.* 131: 868, 1947.
16. Lahey, F. H., and Hoover, W. B.: Injuries to the Recurrent Nerve in Thyroid Operations, *Ann. Surg.* 108: 545, 1938.
17. King, B. T.: A New and Function Restoring Operation for Bilateral Abductor Cord Paralysis, *J. A. M. A.* 112: 814, 1939.

18. Shirer, J. W.: Modification of the King Operation for Bilateral Vocal Cord Paralysis, *Ann. Surg.* **129**: 617, 1944.
19. Kelly, J. D.: Supplementary Report on Extralaryngeal Arytenoidectomy as Relief for Bilateral Abductor Muscular Paralysis of Larynx, *Ann. Otol., Rhin., & Laryng.* **52**: 628, 1943.
20. McCullagh, E. P., and Ryan, E. J.: Treatment of Tetany With A. T. 10, *Tr. Am. A. Study Goiter*, pp 200-216, 1939.
21. MacBryde, C. M.: Parathyroid Tetany, *Surgery* **16**: 804, 1944
22. Bartels, E. C.: Thiouracil and Allied Drugs in Hyperthyroidism, *New England J. Med.* **238**:6, 1948.



## CHAPTER 23

# EXTREMITY

### Infections

Successful management of infections of the extremities demands the closest attention; serious and permanent loss of function and crippling may easily result from delayed or improper care of an initially minor infection.

Cellulitis in the superficial soft tissues is not treated by incision until localization or fluctuation occurs, unless the infection involves a closed space such as the finger tip or a fascial space. Care of diffuse pyogenic infection includes absolute rest and elevation of the affected part, use of hot wet dressings, administration of penicillin or the appropriate sulfonamide, and incision and drainage when softening begins. When the infection is situated deeply, however, as in the palmar spaces or the flexor tendon sheaths, external evidence of fluctuation does not appear. In such cases prompt incision under general anesthesia is performed to relieve the tension due to inflammatory edema, which may obstruct the blood supply and cause ischemic necrosis of the involved tissues within a few hours. Incisions must be properly placed and of adequate extent to afford satisfactory drainage; improper or insufficient incision will encourage spread of infection, damage to previously uninvolved structures, scarring with later restriction of function, and even loss of part of the involved extremity.

Certain fundamental principles of treatment are well known and universally observed. Unless in the superficial subcutaneous tissues, infections of the hand or foot are incised and drained under general anesthesia; local anesthesia is inadvisable because it may encourage further spread of infection and because it does not block painful impulses sufficiently to permit adequate incision. Soaking of the infected part in warm water for thirty minutes before operation will soften the skin and facilitate incision. The type of drain used depends upon the area infected; a shallow wound is packed lightly with petrolatum gauze, while a deeper infection is drained with a strip or two of rubber tissue. Coarse-

meshed gauze, either dry or greased, is never used for drainage; all gauze drains or packs must be fine-meshed to prevent adherence to the tissues. Tight packing and use of rubber tubing are inadvisable; interference with drainage or pressure necrosis may result. Drains should not be left in contact with avascular structures such as tendons or nerves; tendon sheath infections, for example, are drained by adequate lateral incision of the sheath and insertion of a soft rubber tissue drain down to the opening in the sheath but not against the tendon. Through-and-through drainage across a tendon is never employed; such drainage is likely to cause pressure necrosis and sloughing of the tendon. For the same reason through-and-through drainage is never used for infection of the deep fascial spaces of the hand.

Voluminous hot wet dressings (p. 472) are applied loosely with the extremity in the position of function. Constant hot soaking is continued for two to three days. The drains are then removed and hot wet dressings continued for another day or two, until the acute general and local reactions have subsided. Dry dressings are substituted at this time, with a light aluminum or plastic splint to maintain the position of function. The infected extremity at this stage is soaked in a tub or basin of warm water for thirty minutes three times daily with all dressings removed and is exercised gently during soaking. After each soak the extremity is placed on a sterile towel and dried at 90 to 95° F. by radiant heat from a lamp, with care to avoid overheating. All soaks are stopped as soon as possible, to prevent maceration of the damaged tissues. Physical therapy, including active and gentle passive motion, is begun promptly when infection has subsided.

Drains are used in soft tissue infections to prevent pocketing and to allow outflow of pus and exudate as long as active infection and resolving cellulitis are present. When inflammation has subsided and all collections of exudate have been evacuated, the drains should be removed. As a rule, drains are not required for more than three or, at most, four days in infections of the soft tissues or fascial spaces of the distal extremity. Flow of pus will continue, however, as long as the drains are left in place, since they act as infected foreign bodies. Constant irritation of the damaged tissues by prolonged draining causes a profuse outpouring of seropurulent fluid; in many cases also an exuberant

proliferation of edematous infected granulation tissue appears, and osteomyelitis may develop in the underlying bone. Removal of the offending drain and cleansing of the dirty wound will be followed by rapid healing, although proportionately increased scarring can be expected. It is well, therefore, to remove drains as soon as they have served their intended purpose.

### **Peripheral Vascular Disease (Chronic Occlusive Arterial Disease)**

The chief aims of treatment in peripheral arterial occlusive disease include preservation of life, relief of pain, and restoration of useful function in the affected limb. The degree to which preservation of the limb is possible depends upon the extent of disease, the presence of complicating infection, the cooperation of the patient, the methods of treatment used, and the response to treatment. Prolonged confinement to bed or hospital is necessary in most cases, and accurate clinical judgment is required to evaluate the degree of circulatory insufficiency, the possibility of improving the blood supply, and, in unfavorable cases, the optimum time to operate and the proper anatomic level for amputation. Frequently, the measures employed in preoperative care are identical with or are continuations of measures employed in conservative treatment and will vary according to the type and degree of disease present. For this reason the following discussion will be of a general nature.

**History.**—A careful history is indispensable. The patient is questioned about the duration, degree, and regularity of occurrence of intermittent claudication, the presence of paroxysms of rest pain (due to ischemic neuritis) during the night, the presence of painful ulcers or persistent superficial infections on the affected extremity, and the occurrence of noticeably abnormal local color and temperature changes.

**Physical examination** includes not only a thorough study of the diseased extremity, but also a complete general examination. Laboratory work should include urinalysis for albumin and sugar, a fasting blood sugar determination and glucose tolerance test if diabetes is suspected, electrocardiograms and chest x-rays if indicated, a Fishberg urinary concentration test, and the usual complete blood count. In general, arteriosclerotic vascular

occlusion occurs in patients over 60 years of age, although if clinical diabetes is present, atheromatous arterial changes tend to occur from five to ten years earlier. Buerger's disease (thromboangiitis obliterans) characteristically begins before the age of 40, rarely if ever having its onset in patients over 50 years.

**SKIN COLOR AND TEMPERATURE.**—The color and temperature of the skin depend directly upon the rate of flow and the oxygen content of the blood in the superficial vessels. In the presence of normal arteriolar blood flow, elevation of an extremity will produce pallor and cooling of the skin, while dependency will induce a normal pink color with increased warmth. Similarly, increase of arteriolar flow by increasing the environmental temperature will raise the skin temperature and cause reddening; decrease of arteriolar flow by reducing the environmental temperature will cause cooling and pallor of the skin. Normal variations in skin color and temperature under varying circumstances should be completely familiar before examination of the patient with peripheral vascular disease is undertaken.

Occlusive arterial disease causes decreased arteriolar blood flow in the affected extremity. The skin therefore is cooler than normal, whether the limb is elevated or dependent. When the extremity is elevated, the emptying of the capillaries and venules in addition to the decreased arteriolar flow will produce abnormally marked pallor and coldness. Such changes may be generalized and extensive or may be patchy and restricted to small irregular areas or to phalanges in which the terminal circulation is inadequate. If the extremity is then allowed to hang down in a dependent position, the pallor slowly disappears as the small superficial vessels fill, the rate of color return depending upon the rate of arteriolar blood flow. In a dependent limb with insufficient blood supply, the capillaries fill and dilate, the return flow through the venules is slowed still further, and the stagnating blood is relieved of more of its oxygen. A dusky color results, the degree of progression from pink to dark purple depending upon the degree of interference with normal flow. Such effects may be due at least in part to arteriolar spasm; it is imperative to determine how much of the circulatory deficiency is due to organic change and how much to vasospasm.

Obstruction of venous drainage in an extremity with normal arterial channels, as in deep thrombophlebitis, also will produce

cyanotic discoloration, but the widespread and diffuse distribution of the color change, the filled peripheral veins, the warm skin, the edema, and the typical history will make the diagnosis apparent.

Examination for skin color changes should include all four extremities. With the patient supine, both legs are held vertically upward for two minutes, the feet and ankles being exercised actively. Careful inspection is made, with comparison of the two extremities, and areas of mottling or abnormal pallor are noted, particular attention being paid to each of the toes. The patient then sits upright with the legs hanging over the edge of the table. Areas of persistent pallor or of mottling are noted, as well as the degree and extent of rubor, cyanosis, and decreased skin temperature. Definitely abnormal postural skin color changes are diagnostic of occlusive arterial disease, the degree of change being proportionate to the degree of circulatory deficiency. Time required for return of color is noted in seconds and serves as a rough indication of the degree<sup>1</sup> of circulatory damage; normally, color should return to the dependent limb within five or ten seconds. If color has not returned within fifteen seconds, a moderate deficiency is present; if thirty seconds are required, the deficiency is marked; if color has not returned to all parts of the limb within forty-five to sixty seconds, the circulatory deficiency is severe and impending gangrene is likely.

Skin temperature is not a reliable index of circulatory efficiency; air and body temperature, humidity, clothing, exercise, rest, position, smoking, alcoholic drinks, drugs, ingestion of food, nervous excitement, and various other factors may affect the skin temperature to a considerable degree. Patchy areas of coldness and differences in local temperature are of more significance. Under basal conditions, a difference of 2 to 4° F. between symmetrical areas on the two sides indicates a definite decrease in arteriolar flow on the cooler side, due either to organic or reflex occlusion. For practical purposes skin temperature can be estimated *satisfactorily by touch*, the dorsal and ulnar surfaces of the examining hand being somewhat more sensitive to differences than the palmar surface. Skin thermometer determinations are not generally made in clinical practice, although such measurements under basal conditions may be useful in evaluating the effect of regional sympathetic block.

**ATROPHIC CHANGES**—The skin and skin appendages show typical atrophic changes in patients with chronic peripheral vascular disease. The nails become thick, opaque, horny, and heaped up, calluses and corns are more likely to develop, with cornification of the surrounding epithelium, and the skin itself in the area of decreased blood supply becomes thin, atrophic, darkened in color, and more susceptible to trauma. Small lesions and scratches fail to heal and persist as painful, indolent, open wounds. Minor nicks incurred during trimming of nails and calluses tend to become infected and may give rise to chronic ulcers, spreading cellulitis, deep-seated fascial space infections, and even incipient or progressive gangrene. In any patient with chronic occlusive arterial disease the earliest abnormal postural color change and the first signs of gangrene typically appear in the distal phalanges around the nail margins, where arteriolar circulation is terminal and where minor injuries are most likely to occur.

Atrophy of muscle and subcutaneous tissue takes place slowly as the blood supply diminishes and exercise is restricted. The affected limb becomes weaker and may be smaller and somewhat shrunken in appearance.

**ARTERIAL PULSATIONS.**—Arterial pulsations afford confirmatory evidence of impaired circulation, although in occasional cases one or more of the distal arteries may not be palpable because of anomalous location. Calcification in the arterial wall does not always indicate occlusion of the lumen; in Mönckeberg's sclerosis, the medial coat may be extensively calcified with little intimal change or decrease in lumen, while in atheromatous sclerosis, with fibrosis of the media and extensive plaque formation in the intima, the artery sometimes may be effectively blocked and yet show little hardening on palpation. Both types of sclerosis may be present at the same time, however.

**Diagnostic Tests.**—In general, a careful history and physical examination will permit evaluation of the degree of disease, prognosis for improvement and restoration of function, and selection of treatment best adapted to the individual patient.

*Arteriography* and *venography* by injection of radiopaque media have been advocated but provide little additional information; in fact, technical errors, normal variations in the vas-

cular channels, and temporary vasospasm will produce unexpected changes in the roentgenograms that may be interpreted incorrectly as evidence of vascular occlusion. Except in the hands of experienced investigators, such studies are of uncertain value. The *plain x-ray* of the thigh and leg will show arterial calcification of moderately advanced degree. Here, too, evidence of calcification does not necessarily indicate obstruction of the lumen; the calcified medial coat in Mönckeberg's sclerosis typically appears as a long, continuous shadow, while the much more significant calcified atheromatous intimal plaques show as smaller irregular patchy areas of less marked opacity. Frequently little or no calcification may be seen on x-ray even in extremities with advanced gangrene.

The *oscillograph* is designed to pick up the slight changes in volume of the limb which occur with each arterial pulsation, operating on much the same principle as the sphygmomanometer. The practical value of oscillography is seriously limited by the fact that it will not show the presence or the progressive increase of collateral circulation during successful conservative therapy.

Histamine, when introduced intracutaneously, produces localized capillary and arteriolar dilatation, with exudation of plasma from the relaxed small vessels. Visible effects include the appearance of a circumscribed area of erythema and a wheal at the site of injection. This effect has been utilized clinically as the *histamine flare test* for peripheral circulatory efficiency. The test is performed<sup>1</sup> by placing a single drop of histamine acid phosphate solution (1:1,000) at various locations on the affected limb (dorsum of foot, above ankle, middle of leg, below knee, above knee) and pricking the skin several times through each drop as in vaccination. Progress of the wheal can be followed better by palpation than by inspection; normally it appears within two and a half minutes, is well-developed in five minutes, and reaches its maximum within ten minutes. Development of the wheal is retarded if circulation is deficient. The test is not constantly reliable, however, and adds little information to that obtained by clinical examination alone.

The *saline wheal test* is based on the fact that fluid injected intradermally diffuses more rapidly when tissue tension is low, as in vascular deficiency or actual gangrene, than when tension

and circulatory flow are normal. This test also is affected by many variables, which detracts from its clinical usefulness. It is performed by injection of 0.2 c.c. of sterile normal salt solution intradermally to form a visible wheal at intervals two or three inches apart, from the dorsum of the foot to the lower thigh. The wheals are inspected at intervals of five minutes. Normal duration of the wheal is forty-five to sixty minutes; disappearance within twenty-five to thirty minutes indicates circulatory insufficiency, disappearance within ten to twenty-five minutes indicates serious circulatory impairment with threatened gangrene, and disappearance within five to ten minutes signifies actual or impending gangrene. Persistence of the wheal is prolonged by the presence of edema, which therefore detracts from the value of the test.

*Block of the regional sympathetic ganglia* is used both in diagnosis and in treatment. Procaine block of the second to fourth lumbar or the upper thoracic sympathetic ganglia, as indicated, will relieve the arteriolar spasm frequently associated with peripheral vascular disease, especially when ischemic neuritis is present, and will often result in an immediate increase in blood flow to the extremity. Elevation of skin temperature, improvement of skin color, and alleviation of pain will follow to a variable degree. For proper interpretation of the effects of sympathetic block, the procedure should be done once or preferably twice daily for several days, with examination of the extremity under basal conditions. If a definite rise in skin temperature or an evident clinical improvement results, it is probable that sympathetic ganglionectomy will be of value.

**Treatment.**—Patients with peripheral vascular disease are often old, discouraged, and in poor general condition as a result of prolonged pain, restriction of activity, lack of rest, and malnutrition. Whatever local treatment is necessary, every effort should be made to improve the psychologic outlook and the nutritional state. Frequently it is possible to attain enough improvement by conservative measures alone to permit restricted use of the extremity for another year or two; in other cases removal of small gangrenous areas may be sufficient. Occasionally the pain from ischemic neuritis in a hopelessly anemic extremity will be so severe that the patient will gladly



consent to amputation without further delay or will even demand it. Very often too the combination of gangrene and spreading infection in an arteriosclerotic extremity will be so resistant to conservative therapy that prompt amputation becomes necessary to save life.

Although occlusive arterial disease is irreversible and progressive, it develops slowly and with asymptomatic intervals of varying duration. A worth-while degree of clinical improvement and postponement of terminal gangrene often can be attained by increasing the collateral circulation. The capacity for developing accessory vascular channels is most marked in younger people, who also have a greater capacity for tissue repair. Conservative therapy therefore is more uniformly successful in Buerger's disease, which occurs in younger age groups, than in atheromatous arteriosclerosis, although surprisingly good results sometimes can be achieved even in the latter case.

When gangrene is absent or involves only one or more toes and no infection is present, conservative treatment is tried for three or four weeks. If definite improvement has not occurred within this time, amputation is performed. Frequently an uninfected gangrenous toe may be allowed to separate and slough away spontaneously if circulation in the remainder of the foot is satisfactory; surgical amputation of a dry gangrenous toe under these circumstances, although quicker, is more likely to leave a nonhealing wound.

When gangrene involves the dorsum of the foot at the base of the toes or has spread to an even higher level, or when uncontrollable pain due to ischemic neuritis is present, amputation is advisable but not necessarily as an emergency. When gangrene and infection are coexistent in an extremity, an attempt is made to control the infection by immobilization of the limb in a horizontal position, administration of the appropriate chemotherapeutic or antibiotic agent in full dosage, and other general measures as indicated, such as control of diabetes. Hot wet dressings, dry heat, and elevation of the limb are not used in treatment of infected gangrene; these measures will speed the gangrenous process and encourage the spread of infection. Incision and drainage is performed when indicated, but with the greatest care; ill-advised trauma to barely viable tissues will precipitate

gangrene. If the infection subsides promptly, the area of threatened gangrene tends to diminish and conservative measures may become possible. On the other hand, if infection and gangrene continue to spread, guillotine amputation is done without further delay or the limb is refrigerated until the general condition of the patient can be improved sufficiently to withstand operation.

**CONSERVATIVE MEASURES.**—Complete bed rest is ordered, with a cradle to support the bedclothes. No heat is used, either by hot packs or by light bulbs. Although heat produces vasodilatation, it also increases the cellular activity and rate of tissue metabolism; the impaired circulation may be insufficient to meet the heightened oxygen requirements. Cold applications or refrigeration also are not used therapeutically; reduction of temperature lowers the oxygen requirement but decreases the already insufficient blood supply. The extremity is kept horizontal or slightly lowered, according to the position of maximum comfort; elevation of the limb will add to the vascular deficiency. Pressure of the heel against the bed may cause blistering and gangrene; the leg is supported on a pillow high enough to prevent contact of the heel with the bed. Another pillow is placed at the foot of the bed to maintain ankle flexion and prevent foot drop.

No tobacco in any form is permitted; nicotine has a well-marked tendency to produce or intensify arteriolar spasm, particularly in Buerger's disease. Alcohol, however, has a vasodilating effect; whiskey in small to moderate amounts each day may be definitely beneficial. Tea and coffee, which exert a mild vasodilating action, are permissible if no medical contraindication exists.

High protein, high carbohydrate, low fat, high vitamin diet is ordered, with full therapeutic dosage of vitamins A, B complex, and C. Although a low cholesterol diet is of little value when arteriosclerosis is sufficiently advanced to produce symptoms, it may help at least to keep the patient's attention constantly upon care of his condition. Essentially, a low fat, low cholesterol diet<sup>2</sup> eliminates eggs, cream, butter, salad dressing, olives, animal fats, fried foods, gravy, and internal organs such as brains, liver, kidney, and sweetbreads; vegetable fats such as oleomargarine are permissible and should be supplemented with vitamin A.

Postural exercises, designed to improve the collateral circulation, probably are of more value in early Buerger's disease than in arteriosclerosis. The extremity is elevated on a support at 45 degrees for the minimum time necessary to produce blanching (one-half to two minutes), then is held in a vertically dependent position until return of color has reached its maximum (two to four minutes), and finally is placed on the bed horizontally or in the position of greatest comfort for three to five minutes. The cycle is repeated without interruption for an hour several times daily. Special types of apparatus have been advocated to accomplish alternating venous emptying and congestion as a means of increasing collateral circulation; these methods include the oscillating bed, the pneumatic cuff for intermittent venous hyperemia, and the Pavex (passive vascular exercise) machine for alternating suction and pressure. Of these methods, Buerger's exercises are of the most constant value, although they all are widely used. Neither Buerger's exercises nor any apparatus for intermittent venous compression should be employed when visible gangrene or infection is present, because of the danger of increasing the spread of the process.

Foreign protein fever therapy is favored by many as a means of inducing maximum vasodilatation temporarily, especially in Buerger's disease, although it is not advisable in the presence of cardiac disease, hypertension, or infection. Typhoid vaccine is usually employed, in dosage sufficient to cause a temperature rise to 101 to 102°F., without a chill or severe systemic reaction. An initial dose of 5,000,000 organisms<sup>1</sup> may be injected intravenously and repeated every two to three days for eight to twelve doses, increasing each dose as necessary to provoke the desired response.

Various drugs have been advocated for treatment of early peripheral vascular disease. Good results have been claimed in treatment of Buerger's disease by intravenous injection of sodium chloride,<sup>4</sup> administered as 3 to 5 per cent solution in sterile distilled water in doses of 300 c.c. every two days for several months. After this time the interval between doses is gradually increased. During administration care is taken to avoid leakage of the strongly hypertonic solution into the tissues. An average of ten minutes is required for injection of the full dose, the rapid ad-

ministration producing peripheral vasodilatation and a sensation of warmth. The value of this treatment has not been established. Deproteinized pancreatic tissue extract occasionally serves to relieve the pain of intermittent claudication, perhaps by improving the muscle metabolism; no beneficial effect on the failing circulation can be expected. This drug is given intramuscularly in doses of 5 c.c. daily for ten days, then 3 c.c. every other day for two to three weeks, and then at slightly increased intervals for another month. Ethyl ether, 25 c.c. in 1,000 c.c. of normal salt solution, slowly injected intravenously once daily for two courses of twelve injections each as suggested by Katz<sup>6</sup> will relieve pain and promote temporary circulatory improvement in occasional cases. Sodium tetrathionate, originally recommended by Theis and Freeland,<sup>4</sup> is said to reduce the viscosity and clotting tendency of the blood and therefore to be of value during the acute episodes<sup>7</sup> of Buerger's disease. It is administered intravenously in a dose of 0.6 Gm. in 10 c.c. of sterile distilled water, repeated three times weekly for several weeks. Tetraethyl ammonium chloride, when injected intramuscularly or intravenously, is said to block the autonomic ganglia<sup>8</sup> temporarily; its possible place in diagnosis and management of peripheral vascular disease has not yet been established. Shute and associates<sup>20</sup> have claimed promising results in treatment of early peripheral vascular disease and of thrombosis and thrombophlebitis by administration of alpha-tocopherol (vitamin E) in repeated doses of 200 to 300 mg. daily. The administration of anticoagulants such as heparin and dicumarol is obviously useless because of the chronicity of the disease.

Repeated procaine block of the regional sympathetic ganglia is of little or no therapeutic value in chronic occlusive arterial disease but is used as a therapeutic test (p. 763). Regional sympathetic ganglionectomy is most useful in treatment of early Buerger's disease,<sup>7</sup> acute arterial embolism, or following vascular surgery,<sup>6</sup> although some improvement can be achieved in early arteriosclerotic disease of the lower extremity<sup>19</sup> when arteriolar spasm is a factor<sup>22</sup> in promoting the circulatory deficiency. It is of no value if gangrene is already present or if the collateral circulatory channels are insufficient; little benefit can be expected from sympathectomy in patients over 50 years of age and none in patients older than 60 years. Such measures as ligation of the

main venous channel of the extremity, division or alcohol injection of the cutaneous nerve peripherally, and periarterial sympathectomy have been employed to increase circulation or to decrease pain but are of little or no proved value.

Local ulcerations and areas of dry gangrene are treated expectantly. General measures to improve circulation are continued, local pressure is prevented, and as little as possible is done to the lesion to avoid trauma to the dangerously avascular surrounding skin. Antiseptic applications, which may cause irritation and coagulative necrosis, are contraindicated; ointments containing penicillin, nitrofurazone, or tyrothricin are acceptable, however. Application of red blood cells in powder or paste form has been advocated. Best healing, of course, is obtained by improvement of blood supply; other measures are only palliative.

#### AMPUTATION.—

*Preoperative Care.*—When gangrene is present without infection (*dry gangrene*), amputation can be postponed for trial of conservative therapy and for accurate choice of level of amputation. Conservative amputation is often possible in Buerger's disease, in which an adequate collateral circulation may be developed. Removal of a gangrenous toe or portion of a foot is rarely successful in the more common arteriosclerotic gangrene, however; necrosis will develop in the wound and necessitate reamputation at a higher level. Amputation below the knee for arteriosclerotic gangrene of the foot is still advocated at times but has been generally abandoned in favor of supracondylar amputation. If below-knee amputation is performed in such cases, it is wise to drape the thigh also so that amputation can be performed above the knee if the vessels at a lower level prove to be occluded.

When infection is present (*wet gangrene*) and a trial of conservative measures has failed to prevent its progression, amputation may become necessary as an emergency measure to save life. Although some effort is made to control the metabolic disturbance in diabetic patients with infected gangrene (p. 266), operation is not delayed for more than a few hours for this reason if spreading cellulitis and sepsis have appeared. The most important consideration is the immediate removal of the necrotic infected

limb in such patients; administration of penicillin is begun, an infusion is given, and a blood transfusion is prepared. Although perhaps not strictly necessary, it is well to administer prophylactic doses of tetanus and gas bacillus antitoxins before operation. The usual preoperative medication is given and the most suitable anesthetic chosen. As a rule, a gangrenous extremity with spreading infection is removed either by guillotine or open circular amputation, with skin traction applied immediately after operation and continuing during the postoperative period. When the blood supply and the extent of infection will permit, open amputation may be done below the knee, with closed supracondylar amputation as an elective procedure later. If the process is dangerously extensive, however, open amputation is done primarily at the supracondylar level.

*Refrigeration.*—When the patient with advanced or infected gangrene is too seriously ill to be an acceptable surgical risk, toxicity and pain can be reduced by packing the diseased limb in ice, either with or without a proximal tourniquet. Much discussion has arisen concerning the best technique for this procedure and concerning the resulting physiologic effects.

Reduction of tissue temperature by refrigeration produces certain definite results: (1) the rates of cellular metabolism and oxygen utilization are decreased, (2) the velocity of blood flow is decreased, (3) the rate of lymphatic absorption is diminished, (4) the conductivity of nerve endings and nerve trunks is depressed or abolished, (5) the inflammatory response to tissue irritants or bacterial infection is reduced, and (6) the progress of wound healing is delayed. Refrigeration of a painful gangrenous limb therefore can be used to relieve pain, to produce surgical anesthesia, to delay the progress of infection and gangrene, and to diminish the absorption of toxins from the diseased area. Time can be gained to improve the surgical acceptability of a critically ill patient; if refrigeration is maintained properly, operation can be postponed for a day or more.

If the circulation is completely blocked in a severely crushed or gangrenous unrefrigerated limb by means of a tourniquet placed well above the lesion, the absorption of toxic products and the local loss of plasma will be stopped. Extreme pain will result, however, and the gangrene and infection will continue to progress. If the tourniquet remains for more than six to eight

hours, such a limb must be amputated without preoperative release of the constriction; removal of the tourniquet after prolonged application will flood the circulation with toxins and produce a shocklike picture. Refrigeration of the damaged limb, however, will permit prolonged use of a tourniquet without pain, combining the advantages of refrigeration with the certainty of complete block of lymphatic and vascular absorption of toxins.

Opinions differ concerning the viability of tissues treated by refrigeration and by tourniquet block. Allen,<sup>11</sup> who first explored the clinical possibilities of the procedure, maintains with Crossman<sup>12</sup> that viable tissues will not be damaged by refrigeration with or without a tourniquet if cooling does not go below 40°F. For preparation of a poor-risk patient for operation, these authors advise application of icebags to surround the entire extremity to a level well above the site of the tourniquet, which is applied after refrigeration anesthesia has developed. Elastic gum rubber tubing (1.25 cm.) is used for the tourniquet, two complete turns being applied tightly. The two ends are held by a clamp, with a gauze pad beneath to protect the skin. Before application of the tourniquet, the leg is elevated to drain out the blood, if infection is present, this step is omitted. Refrigeration is continued, a temperature near but not below 40°F. being maintained at skin level. Anesthesia is complete within two to five hours. Operation may be performed at this time or delayed as long as desired if refrigeration is maintained properly. In the operating room the icebags are kept in place until preparations are complete; the extremity is then lifted out, cleaned, and draped. Amputation is made at a level several inches below the tourniquet, without necessity for supplementary anesthesia. When the limb has been amputated, the tourniquet is released, blood vessels are ligated, and the incision is closed. Richards<sup>13</sup> also remarks that the use of refrigeration with a tourniquet above the chosen site of amputation permits operation in a bloodless and completely anesthetic field without additional anesthesia.

Cayford and Pretty<sup>14</sup> agree to the value of refrigeration for producing anesthesia, reducing toxic absorption, and decreasing operative shock but feel that use of a tourniquet is not necessary and may be followed by delayed wound healing. These authors have suggested another simple method of refrigeration: An in-

verted leg cradle is lined with rubber sheeting, extending from the region of the ischial tuberosity downward over the foot of the bed into a pail on the floor. The bottom of the cradle is covered with a layer of chopped ice four inches thick, the limb is placed upon the ice, and enough ice is added to surround the entire extremity with a layer four inches thick from toes to upper thigh. Drainage of water is facilitated by elevation of the head of the bed, and melted ice is replaced at frequent intervals. Refrigeration for five hours is necessary to produce sufficient anesthesia for thigh amputation but can be continued indefinitely if indicated. A tourniquet can be applied shortly after refrigeration is begun or may be omitted, according to the preferences of the surgeon. The extremity remains packed in ice until ready for cleaning, draping, and amputation in the operating room. After operation a pressure dressing is applied to the stump and three icebags are used to continue cooling, one icebag being removed each day.

Large and Heinbecker<sup>15</sup> recognize the advantages of refrigeration but cite experimental evidence to show that refrigeration is followed by delayed wound healing, increased risk of infection, and tissue damage proportionate to the duration of cooling. Although use of a tourniquet is stated to prolong the viability of the refrigerated ischemic tissues at the site of amputation, the ill effects of cooling are still to be expected. These authors therefore favor refrigeration nearly up to the knee, application of a tourniquet below the knee in the refrigerated zone two to four hours later, and amputation above the knee under general or spinal anesthesia after twenty-four hours, when the general condition of the patient has been sufficiently improved. Amputation is performed through an unrefrigerated area and normal prompt healing can be expected.

Regardless of which technique is employed, certain general principles of refrigeration should be observed. Refrigeration will not save a nonviable limb but will simply relieve pain, reduce toxic absorption, and gain time for improvement of general condition. Neither salt nor "dry ice" (solid carbon dioxide) is ever added to the crushed ice; ice alone will reduce the limb temperature to 40° F., which is fully sufficient. Further reduction of temperature will cause freezing of the tissues, with permanent destruction. Also, if a tourniquet is applied to a refrigerated gangrenous limb, it should not be released until after amputation has been per-



formed, or sudden absorption of large quantities of toxic substances will take place.

*Postoperative Care.*—When the stump is closed by suture, drainage can be accomplished either by loose closure of the flaps or by use of a strip of rubber tissue in the angle of the wound. Gauze dressings are applied and the stump is bound snugly but not tightly with an elastic bandage to minimize postoperative edema. The bandage is applied from below upward to prevent venous congestion from developing during bandaging. Following amputation below the knee, a posterior splint of plaster or wood is applied to prevent postoperative flexor spasm from producing flexion contracture. Drains are removed after forty-eight hours. When no drains are used, the original dressing is left in place for seven to ten days unless evidences of hemorrhage, infection, or excessive drainage appear. The patient is allowed out of bed in a wheel chair on the second day if no contraindications exist, and a full diet is ordered promptly. Penicillin may be given for several days for prophylaxis against infection.

Following guillotine or *open* amputation, the stump drains freely and frequent change of dressing is necessary. Because the wound edges are unsutured, skin margins soon become fixed in retraction by fibrosis and scarring and cannot subsequently be freed enough to cover the stump. For this reason some form of skin traction should be applied at the close of operation or within thirty-six hours at the latest. Continuous traction is maintained until the open end of the stump has been entirely covered with normal skin and healing is complete. Depending on the level at which open amputation was performed, final healing should occur within two to four weeks. Every effort is made to secure closure of the stump by skin traction; skin grafts will not suffice even as a temporary covering until secondary revision can be performed.

Skin traction can be applied either with adhesive tape straps or with circular stockinet of the appropriate size. Following amputation, a fine-meshed gauze dressing is placed upon the wound surface and the skin of the extremity is painted around its entire circumference with evaporated compound tincture of benzoin or liquid adherent, beginning four to five inches above the level of amputation and extending to within one inch above the wound edge. The upper end of a portion of stockinet (sixteen to twenty inches long) is slipped over the stump far enough to cover

the painted area of skin, to which it is allowed to become adherent. Dressings are packed lightly inside the stockinet against the wound, a spreader and rope are tied in the lower end of the stockinet, and the traction cord is carried over a pulley at the foot of the bed. Although less satisfactory than stockinet, adhesive tape straps may be used; one strap is affixed longitudinally to each aspect of the extremity and the four straps are attached to a spreader and traction cord. The inner surface of the lower portion of each strap is covered with adhesive tape, smooth side out, to prevent adherence to the wound and the dressings. Neither stockinet nor tape should be allowed to adhere to the skin for approximately an inch above the wound edge; the free margin of skin must be able to curl downward over the stump when traction is applied rather than remain adherent to the traction apparatus, which would then actually pull it away from the wound.

Additional fluffed gauze is placed over the stump outside the traction dressing and an elastic bandage is applied snugly from below upward to minimize edema. A splint is not necessary, although the extremity may be supported with a small firm pillow proximal to the end of the stump. The patient is encouraged to move about freely; close attention is paid to maintenance of firm but comfortable traction at all times. The dressings are changed as necessary simply by releasing traction, removing the spreader, and renewing the gauze packs. The traction dressing itself can be removed and replaced without necessity for analgesic medication other than a dose of morphine. Care is taken to avoid contamination; change of traction straps or stockinet should be done in the operating room.

### Arteriovenous Fistula

The physiologic effects which result from an abnormal arteriovenous communication depend upon the size and location of the vessels involved, the size of the fistula, the volume of blood passing through the opening, and the duration of the disease. Although congenital lesions of this type occur, the commonest form of arteriovenous fistula is the type secondary to trauma, with damage to the walls of an artery and the accompanying vein or veins.

Diversion of arterial blood directly into the venous channels causes an initial fall in arterial blood pressure and rise in venous pressure, with corresponding increase in the pulse rate and cardiac output. Capillary flow distal to the fistula is decreased, the arterial blood supply improves with time as collateral vessels develop, but venous congestion remains. If the fistula is large, evidences of chronic venous stasis appear, with edema, dusky pigmentation, venous distention, and chronic indurative ulcerations. In some cases the total blood volume increases, possibly in compensation for the drainage of blood out of the arterial circulation through the fistula. The systolic blood pressure finally rises to a normal level, although the diastolic pressure remains depressed. Cardiac enlargement may develop, probably from dilatation rather than hypertrophy, since normal cardiac dimensions are restored after operative closure of the fistula.

Characteristic evidences of arteriovenous fistula include signs of chronic venous congestion distal to the lesion, with pain and a variable degree of interference with function in the affected extremity. A thrill is palpable over the lesion and a continuous machinery-like bruit is audible upon auscultation, increasing in intensity during systole and diminishing but still present during diastole. Temporary closure of a large arteriovenous fistula by digital pressure will produce the characteristic Nicoladoni-Branham bradycardiac reaction, marked by a prompt rise in blood pressure and fall in pulse rate. Holman<sup>16</sup> states that these effects probably are due to sudden distention of the left heart and aorta by the backing up of a large volume of blood which previously was drained through the fistula. The consequent sharp rise in blood pressure stimulates the cardiac depressor nerve endings in the aortic arch, causing a proportionate drop in pulse rate. These effects persist while the fistula is held closed; release of pressure is followed by immediate restoration of blood pressure and pulse rate to their former levels. Permanent surgical closure of the fistula is followed by the same immediate effects, after which the blood pressure returns slowly to a normal range.

Preoperative studies of the circulation may be of value. An x-ray plate of the chest is made for demonstration of cardiac dilatation and for comparison with a similar x-ray film taken after postoperative circulatory readjustment is complete. The distal

arterial pulsations in the affected limb are noted and compared with those in the opposite normal limb; oscillometric studies also may be made. The venous pressures in the two extremities are compared and the circulation times may prove of interest. Arteriography will permit localization of the lesion, demonstration of an aneurysmal sac if present, and visualization of at least a portion of the collateral vessels.

For *arteriography* of the lower extremity the patient is placed supine with a film under the approximate site of the lesion, and the inguinal area is cleaned and draped. The femoral artery is located by palpation just below the middle of the inguinal ligament and the overlying tissues are anesthetized with procaine. A syringe containing 20 c.c. of Diodrast or Neo-iopax with an intravenous needle (19 gauge) is prepared, and arterial puncture is performed gently. When a strong pulsing backflow of bright red blood is obtained, the artery above the site of puncture is occluded by strong pressure with the fingers and the solution is injected fairly rapidly. The film is exposed as the last of the solution is introduced. Pressure on the artery is maintained until the film has been replaced and then is released for a second or two to allow the dye to be carried further distally. The artery is again occluded, and another roentgenogram is made. Arteriography in the upper extremity is performed similarly, a blood pressure cuff being useful if the fistula is located below the elbow. From 10 to 12 c.c. of the radiopaque medium will suffice for arteriography in the arm. Proper timing is necessary to secure satisfactory arteriograms, especially in the leg, since the dye is carried away so rapidly; one or two seconds delay may spoil the film. Care is taken to avoid spilling the solution into the tissues to avoid local soreness. Although sensitization to these iodine compounds is uncommon, it is a justifiable precaution to test for sensitivity by the conjunctival method before use.

Selection of the optimum time for operation is of the greatest importance; repair of an arteriovenous fistula is not an emergency unless signs of continuing leakage into the tissues appear. Operation is best delayed for at least three months following the primary injury to permit collateral circulation to develop, to allow the hematoma to absorb and the surrounding inflammatory reaction to subside, and to allow scarring and shrinkage of the fistula to take place. While restorative arteriorrhaphy is the

operation of choice when possible,<sup>17-18</sup> quadruple ligation of the artery and vein with excision of the involved segment is most commonly performed. Presence of collateral circulation sufficient to supply the needs of the limb after ligation of the involved arterial channel is therefore indispensable to the success of the operation.

The extent of collateral circulation can be estimated in most cases by clinical examination alone; when doubt exists, the Matas-Moszkowicz test is employed. With the patient supine, a Matas compressor<sup>19</sup> is applied over the artery at or just proximal to the site of the fistula (or aneurysm) tightly enough to block the flow of blood. Complete occlusion of the vessel is confirmed by the absence of bruit on auscultation. The extremity is elevated gently and an Esmarch bandage is applied snugly, beginning at the digits and extending up to the compressor. After several minutes the Esmarch bandage is removed rapidly and the extremity placed horizontally; care is taken not to remove or displace the compressor. Return of blood flow to the extremity takes place through the collateral channels. If a pink flush reaches the digits within one to two minutes, the circulation is adequate; if three minutes or more are required, the collateral circulation is poor and arterial ligation is likely to be followed by gangrene. The results of the test may vary from time to time even in the same patient; repeated determinations are advisable. A compressor with a small head should be used to avoid blocking nearby collateral vessels during the test.

When the collateral circulation is insufficient, some improvement may be attained by repeated procaine block of the regional sympathetic ganglia or, preferably, by sympathectomy. Further delay of operation may be advisable, with attempts to improve the accessory channels by application of the Matas compressor to the lesion several times daily for increasing periods of time. Use of the compressor for this purpose usually is more effective in management of aneurysm than of arteriovenous fistula. If evidence of improvement does not appear after several weeks of such treatment, further attempts will be of little avail.

In the operating room an infusion is allowed to run slowly; since sudden profuse bleeding may take place, from 1 to 2 liters of blood must be available for immediate transfusion, with a

needle already in place for its administration. Efforts are made to secure and ligate even the smallest bleeding vessels when post-operative heparinization is planned in order to avoid the danger of local hemorrhage.

While arteriorrhaphy with reconstruction of the lumen affords the best result in suitable cases, it may be followed by thrombosis. Depression of the clotting time by administration of heparin or of dicumarol<sup>21</sup> until healing has occurred will afford protection against intra-arterial clotting; if anticoagulant therapy is instituted, however, the usual precautions are taken against overdosage and postoperative hemorrhage. Quadruple ligation with excision of the fistula is safe and satisfactory in most cases, although it is often followed by vascular insufficiency, with pain on exercise, coldness and pigmentation of the skin, and atrophy or even gangrene of the extremity.

Following operation loose dressings are applied to maintain warmth but constriction is to be avoided; a light splint may be incorporated in the dressing to prevent motion. The limb is kept in a horizontal position under a cradle, although no heat is applied. Close watch is kept for signs of early postoperative bleeding, deficient peripheral circulation, or late secondary hemorrhage. Activity is restored to the affected limb slowly. Lumbar or dorsal sympathectomy may be performed after operation,<sup>8</sup> if not before, to insure maximum opening of the collateral blood channels when there is some doubt of the competency of the collateral circulation. Sympathetic ganglion block and sympathectomy are performed only when indicated; neither procedure should be used as a routine in all patients requiring vascular surgery.

### References

1. Allen, E. V., Barker, N. W., and Hines, E. A., Jr.: *Peripheral Vascular Diseases*, Philadelphia, 1946, W. B. Saunders Co.
2. Kramer, D. W.: *Manual of Peripheral Vascular Disorders*, Philadelphia, 1940, The Blakiston Co.
3. Barker, N. W.: The Plasma Lipoids in Arteriosclerosis Obliterans, *Ann. Int. Med.* 13: 685, 1939.
4. Samuels, S. S.: *The Diagnosis and Treatment of Diseases of the Peripheral Arteries*, New York, 1936, Oxford University Press.
5. Katz, R. A.: Impending Ischemic Gangrene; New Non-Surgical Therapeutic Suggestions, *New Orleans M. & S. J.* 98: 542, 1946.

6. Theis, F. V., and Freeland, M. R.: *Thromboangitis Obliterans: Treatment With Sodium Tetrathionate and Sodium Thiosulfate*, Arch. Surg. 10: 190, 1940.
7. DeTakats, G.: *The Value of Sympathectomy in the Treatment of Buerger's Disease*, Surg., Gynec. & Obst. 79: 359, 1944.
8. Coller, F. A., Campbell, K. N., Berry, R. L. L., Sutler, M. R., Lyons, R. H., and Moe, G. K.: *Tetra-ethyl-ammonium as an Adjunct in the Treatment of Peripheral Vascular Disease and Other Painful States*, Ann. Surg. 125: 729, 1947.
9. Shumacker, H. B., Jr.: *Sympathetic Interruption in Cases of Trauma and in Post-traumatic States*, Surg., Gynec. & Obst. 84: 739, 1947.
10. DeTakats, G., and Evoy, M. H.: *Sympathectomy for Peripheral Vascular Sclerosis*, J. A. M. A. 133: 441, 1947.
11. Allen, F. M.: *Reduced Temperatures in Surgery. I. Surgery of the Limbs*, Am. J. Surg. 52: 225, 1941.
12. Crossman, L. W., and Allen, F. M.: *Surgical Refrigeration and Preservation of Tissue*, J. A. M. A. 133: 377, 1947.
13. Richards, V.: *Refrigeration Anesthesia in Surgery*, Ann. Surg. 119: 178, 1944.
14. Cayford, E. H., and Pretty, H. G.: *Refrigeration Anesthesia and Evaluation of Amputation Sites by Arteriogram*, Ann. Surg. 121: 157, 1945.
15. Large, A., and Heinbecker, P.: *Refrigeration in Clinical Surgery*, Ann. Surg. 120: 707, 1944.
16. Holman, E.: *Roentgenologic Kymographic Studies of the Heart in the Presence of an Arteriovenous Fistula and Their Interpretation*, Ann. Surg. 124: 920, 1946.
17. Freeman, N. E.: *Arterial Repair in the Treatment of Aneurysms and Arteriovenous Fistulae*, Ann. Surg. 124: 888, 1946.
18. Heringman, E. C., Rives, J. D., and Davis, H. A.: *The Repair of Arteriovenous Fistulas*, J. A. M. A. 133: 663, 1947.
19. Massell, T. B.: *The Fluorescein Wheel Test for Collateral Circulation in the Preoperative Evaluation of Patients With Aneurysms and Arteriovenous Fistulas*, Surgery 21: 636, 1947.
20. Shute, E. V., Vogelsang, A. B., Skelton, F. R., and Shute, W. E.: *The Influence of Vitamin E on Vascular Disease*, Surg., Gynec. & Obst. 86: 1, 1948.
21. Shumacher, H. B., Jr., Abramson, D. L., and Lampert, H. H.: *The Use of Anticoagulants in the Surgery of Aneurysms and Arteriovenous Fistulas, With Particular Reference to Dicumarol*, Surgery 22: 910, 1947.
22. Freeman, N. E., Leeds, F. H., and Gardner, R. E.: *Sympathectomy for Obliterative Arterial Disease; Indications and Contraindications*, Ann. Surg. 126: 873, 1947.

## CHAPTER 24

### GYNECOLOGIC SURGERY

As in other types of surgery, the results achieved in operative gynecology are improved by close attention to the details of preoperative and postoperative care. The average patient in good general physical condition requires little special preparation unless an extensive procedure is planned. Many gynecologic patients, however, are in the older age groups, others are substandard risks because of obesity, nutritional deficiency, or chronic anemia, and others present special problems because of acute or chronic infection or scarring involving the pelvic organs or the urinary tract.

#### Preoperative Care

A detailed history is secured, particularly with respect to the patient's menstrual function, marital state, record of pregnancies, and urinary symptoms. The date, duration, and characteristics of the last menstrual period, the preceding menstrual period, and any intermenstrual bleeding are noted; frequently an accurate diagnostic impression can be reached only by consideration of the type of bleeding and possibility of pregnancy in association with the findings on physical examination. Frequently the vagueness of the complaints and a consideration of the personality of the patient will indicate the need for a psychiatric consultation rather than for a surgical operation. If the pathologic condition is not clear cut and definite, a long and detailed history should be obtained, with particular reference to the completeness of sexual satisfaction, the existence of mental or emotional strain in relations with the husband or other members of the household, and the presence of tension or frustration with respect to outside occupations or interests. Conflicts of these types are all too frequently the basis for symptoms which lead to repeated operations in the hope of finding a cure, with resultant aggravation of symptoms rather than relief. On the other hand, it is never justifiable to label symptoms as functional until after a thorough examination has been made.



A full history is taken of previous operations; the date of operation, type and duration of preceding symptoms, nature of operation, duration of convalescence, and degree of relief are noted. It is always advantageous to secure a summary of the operative notes from the hospital at which the operation was performed, including the date, findings at operation, and a full description of the surgical procedure. Finally, a complete history is taken to determine the possible presence and extent of disease in other systems of the body, particularly the urinary system.

Complete physical examination is performed. If pelvic examination is unsatisfactory because of the patient's inability to relax the abdominal muscles, the examination is repeated under sodium pentothal anesthesia unless enough evidence is present to warrant operation without further confirmation. In the latter case, pelvic examination is performed in the operating room after anesthesia has been induced. When the diagnostic possibilities include ectopic pregnancy or acute pelvic inflammatory disease, the examination should be made as gently and with as little manipulation as possible; rough handling may cause sudden bleeding or spread of infection. When a tentative diagnosis has been reached, the plan of procedure should be discussed with both the patient and her husband if the proposed operation will interfere with the possibility of future pregnancy. In some cases it is best to postpone an elective gynecologic operation until after the patient has completed her family. In any case, after the situation has been explained, permission should be secured to perform whatever operative procedure appears to be necessary in the best judgment of the surgeon after the abdominal cavity has been opened.

As a rule, surgery for pelvic inflammatory disease is not performed until after the infection has subsided and the patient has been afebrile for at least six months. If a thorough bimanual pelvic examination after this interval produces a significant temperature rise within twenty-four hours, operation is again deferred. Surgery performed while active inflammation is present is technically difficult and is likely to result in extension of infection, production of widespread adhesions, and injury to the bowel, with ileus, generalized peritonitis, or fecal fistula. While a slight elevation of temperature following preoperative pelvic examination does not necessarily contraindicate operation,

a moderate to severe postoperative reaction can be expected. The sedimentation rate has been suggested as a good preoperative index of activity of pelvic inflammatory disease, operation to be delayed until the sedimentation rate is normal.<sup>1</sup>

Complicating disease of other organs is investigated fully when present. If there is evidence of cardiac disease or hypertension, an x-ray plate of the chest and an electrocardiogram are secured; exercise tolerance and breath-holding tests also are made. In most cases neither age<sup>2</sup> nor heart disease alone are contraindications to operation; cardiac patients or patients in the older age groups with prolapse or pelvic tumors are made far more comfortable by operation, when possible. A catheterized specimen of urine is examined routinely; when impairment of renal function is suspected, further investigation is made by means of phenolsulfonphthalein excretion, Fishberg concentration, and urea clearance tests, and the nonprotein nitrogen level of the blood is determined. In aged, obese, or debilitated patients, the hippuric acid excretion (Quick), cephalin-cholesterol flocculation, and bromsulfalein excretion tests are of value in detecting deficiencies in liver function. Routine blood studies before major operation should include red cell, white cell, and differential counts and hemoglobin and hematocrit determinations; Wassermann or Kahn tests also are often informative. Bleeding, coagulation, and prothrombin times are determined in patients who give a history of excessive or prolonged bleeding. Cross matching for transfusion, always necessary before major operations or in anemic patients, now includes routine Rh type determination in most hospitals; this procedure must not be omitted if the patient is in the child-bearing age or has had blood transfusions previously.

Aged patients require particularly careful consideration. Before surgery is advised, the possible benefits of operation are evaluated with respect to the expected increase in morbidity and mortality rates due to the effects of age. As a rule, the least taxing procedure that will accomplish a satisfactory result is to be preferred in poor-risk patients; when the life expectancy is short, it is better simply to provide relief for the infirm individual than to strive for complete cure with the danger of increased operative risk.

The average gynecologic patient requires little more than local preparation before operation. When an extensive procedure is planned upon a poorly nourished patient, however, it is well to postpone operation if possible until an improvement in general health can be effected. High protein, high carbohydrate, high vitamin diet (3,000 to 4,000 calories) is prescribed with therapeutic doses of vitamins B complex and C each day, and the patient is urged to take large quantities of fluid. When significant anemia is present, whole blood transfusions are given before operation until the red cell count and hematocrit level are within the normal range, and more blood is secured for transfusion during and immediately after operation. Obese patients, like undernourished patients, have a greater tendency to develop complications; if operation can be delayed with safety, it is often worth while to place the patient on a high protein-low fat reducing diet, with added vitamins.

Oral and upper respiratory tract infections are cleared before operation. Chronic urinary tract infections are treated actively to prevent postoperative acute exacerbation; such infections frequently are found in patients with cystocele or procidentia because of the long-standing presence of residual urine. Before operation for repair of cystocele or uterine prolapse is undertaken, a routine check for chronic cystitis is made; if bladder infection is present, operation is deferred until the infection is cleared.

Efforts are made to clear the vaginal tract of leucorrheal discharge; douches of normal salt solution, mercuric chloride (1:20,000), aqueous Zephiran (1:2,000), or potassium permanganate (1:5,000) are used several times a day for several days before operation. More prolonged treatment occasionally is necessary, chronic cervicitis may require cauterization, with delay of operation until healing, and *Trichomonas* infection or moniliasis sometimes is sufficiently pronounced to warrant a preliminary course of therapy. A sloughing or infected cervical or endometrial polyp may cause contamination during hysterectomy; it may be best to postpone operation until the polyp has been removed and local healing has occurred.

Plastic operations performed on patients still in the menstrual age are done in the first half of the menstrual cycle rather than in the latter two weeks, to allow healing before onset of the

next period. Plastic operations performed on patients past the menstrual age may be much more difficult technically; senile changes develop in the vaginal mucosa after the menopause, with atrophy, thinning, and decreased vascularity. In this state the tissues are fragile, dry, and inelastic; healing is retarded, and postoperative wound infection and separation are more likely to develop. Preoperative use of vaginal suppositories containing estrogenic substance are of definite value in such patients, the vaginal mucous membranes being restored temporarily to their healthy normal premenopausal state. Suppositories containing 0.5 mg. stilbestrol or 2,000 I.U. or more of estrogenic substance are used nightly for three to four weeks before operation and, if indicated, for two or more weeks thereafter.

Bleeding due to endometrial hyperplasia or to anovulatory cycles can often be controlled temporarily by testosterone propionate, 25 mg., administered intramuscularly every two or three days for several doses; the same medication will frequently cause a variable degree of temporary regression in the scattered implants in endometriosis, facilitating operative attack.

Patients scheduled to undergo repair of a rectovaginal fistula or of a perineal laceration which has involved the anal sphincter are kept on a nonresidue soft or liquid diet for a week before and two weeks after operation. Either sulfasuxidine or sulfathalidine is given in full dosage during the same period. Other measures of preoperative and postoperative care do not differ from those outlined previously for surgical repair of the anal sphincter.

As a routine measure in the average case, a tap water enema and a short-acting barbiturate such as Nembutal or Seconal 0.1 Gm. (gr. 1½) are given the night before operation, and nothing is permitted by mouth after midnight. In the morning a similar dose of the barbiturate is given one and a half hours before operation and an appropriate dose of morphine and scopolamine (or atropine) is administered a half hour before induction of anesthesia.

### **In the Operating Room**

Preparation of the patient in the operating room varies according to the preference of the surgeon. In any case it is advisable to shave the entire abdomen and perineum, even though

vaginal operation alone is planned. If laparotomy becomes necessary unexpectedly either as a procedure of choice or of necessity, time is saved and contamination avoided if preparation has already been made. Another measure of primary importance, occasionally overlooked even in the most smoothly functioning operating room, is preoperative catheterization of the bladder. Even though the patient voids before being brought to the operating room, there often is an unavoidable delay before operation is begun, and the bladder may again fill with urine. If catheterization is unthinkingly omitted, the partially filled bladder may be injured when the abdominal incision is made and, in any case, will interfere with performance of the operation. Catheterization then must be done beneath the drapes by an assistant, with the risk of contamination of both the field of operation and the bladder itself. Occasionally, even though properly emptied during preparation, the bladder will become distended during the course of a prolonged operation, particularly if infusions are administered. For these reasons some surgeons prefer to insert a rubber catheter before laparotomy and to tape it to the patient's thigh, insuring drainage until the operation is completed. Before removal of such a catheter, 1 ounce of Mercurochrome (0.5 per cent) or of boric acid (4 per cent) is instilled. Catheterization in the operating room is routine after operation in all procedures during which the bladder might have been injured.

An infusion is started at the beginning of every major operation, so that a blood transfusion can be given without loss of time if necessary. While transfusion is not required in most cases, it is advisable to be prepared to administer blood promptly if an emergency should arise.

### Postoperative Care

Routine measures of postoperative care do not differ from those employed following other surgical procedures of equal extent. Sedation is achieved with morphine, 10 to 16 mg. (gr. 1/6 to 1/4), or with another narcotic in equivalent dosage, to be administered as soon as the patient regains consciousness and becomes restless and uncomfortable. Small or aged patients require proportionately smaller doses of narcotic medication. Additional doses are necessary at intervals during the first two

postoperative days. Although too large or too frequent doses of opiates are inadvisable, enough should be supplied to make the patient comfortable during the day or two following operation; in many cases an uncomplaining patient is allowed to go too long with pain that can and should be relieved. The tendency of morphine to produce nausea in many patients should be remembered. When the postoperative reaction is over, simple analgesics are substituted and a short-acting barbiturate is ordered for use at bedtime each evening if necessary.

Nausea and vomiting disappear in most cases within several hours after recovery from anesthesia. If these symptoms persist, gastroduodenal suction is instituted, the tube being removed when the amount of gastric drainage has become small and peristalsis is beginning to return. Postanesthetic nausea and vomiting sometimes are due to dehydration; prompt administration of an infusion of 1,000 c.c. of dextrose (5 per cent) in distilled water may relieve the distress without necessity for passage of a stomach tube. On the other hand, persistence of vomiting and paresis of the bowel in spite of gastric suction drainage may indicate the need for intubation with a Miller-Abbott tube. Occasionally, mechanical intestinal obstruction will develop following adhesion of loops of small bowel to the rough surfaces left at the field of operation. Evidences of obstruction of this type may not be marked; the symptoms of mechanical block may merge continuously with the symptoms of prolonged postoperative intestinal paresis, which occurs so commonly following abdominal operations. When gastric suction drainage must be continued for more than three or four days and no flatus is passed during this time, the possibility of either mechanical intestinal obstruction or paralytic ileus must be considered and investigated. It is often advisable to introduce a Miller-Abbott tube immediately after operation if extensive adhesions have been divided, large raw surfaces have been left, or active inflammation is present; intubation of the small bowel in such cases may prevent the development of intestinal obstruction.

Insertion of a rectal tube and use of a water and glycerine enema (p. 127) as necessary to encourage evacuation of flatus are routine orders following gynecologic surgery in many hospitals, although neither measure should be used following opera-

tions involving the anal sphincter, the perineum, or the rectum. A large enema is not given in any surgical case until at least five days have passed.

After recovery from anesthesia, the patient's position is changed completely every hour when awake, inhalations of carbon dioxide are given hourly when indicated, deep-breathing exercises are taken under the direct supervision of an attendant, and active exercises of the legs and feet at frequent intervals are insisted upon even though the patient may be reluctant. Many surgeons have adopted the practice of early ambulation following gynecologic surgery, allowing the patient to be helped out of bed from twenty-four to forty-eight hours after operation. Two or three steps are taken with assistance on the first occasion, and the patient is helped to walk a short distance several times daily thereafter; by the fourth or fifth day unsupported ambulation is the rule and the patient is able to go to the bathroom. It is not advisable to allow the patient to sit up in a chair during this time, however. Collins<sup>3</sup> advocates the use of cotton sutures in vaginal plastic operations about the bladder and urethra, stating that patients can be gotten out of bed safely the day after such operations, encouraging spontaneous voiding and rendering unnecessary the use of retention catheters. Although early ambulation apparently shortens convalescence and does not endanger the success of the operative repair, many surgeons still prefer to keep the patient in bed for ten to fourteen days following either laparotomy or extensive colporrhaphy.

An average daily intake of 2,500 to 3,500 c.c. of fluid is maintained. Most of the fluid given by infusion is supplied as dextrose (5 per cent) in distilled water; since the daily salt requirement is satisfied with from 5 to 8 Gm. of sodium chloride, not more than 1,000 c.c. of normal salt solution (0.89 per cent sodium chloride) is given each day. Administration of larger quantities of salt may result in salt retention with subclinical edema and waterlogging of the tissues. Infusions as well as transfusions are given more slowly to aged patients or patients with cardiac disease; if evidences of venous congestion, dyspnea, or pulmonary edema appear, the flow of fluid is stopped at once. Unless the patient is able to take sufficient quantities of fluid by mouth, an accurate record is kept of the fluid intake and output; enough fluid is supplied to keep the total daily urinary output

within the optimum range of 1 to 1½ liters. Blood transfusions are of the greatest value in seriously ill patients or patients with advanced malnutrition.

Urinary retention is particularly frequent following gynecologic operations. Catheterization is performed immediately after operation, and 1 ounce of Mercurochrome (0.5 per cent) is instilled into the bladder to encourage spontaneous voiding subsequently (p. 329). After return to the ward the patient is catheterized every eight hours unless at least 150 to 200 c.c. of urine are passed at a single voiding during each such interval of time. It is not always safe, however, to defer catheterization for so long; the bladder may fill with urine in an hour or two after an infusion is given, and overdistention can develop long before the next scheduled time for routine catheterization arrives. Following operation the sensation of bladder fullness may be entirely absent, especially when narcotics are given for pain; marked overfilling may occur without discomfort, or perhaps simply with a sense of vague lower abdominal distress and general restlessness. The usual measures to encourage spontaneous voiding are employed, although catheterization should not be postponed unduly long. Overflow incontinence also may occur, with voiding of an ounce or two of urine at frequent intervals, the bladder remaining tensely distended despite passage of relatively large amounts of urine in total. Some patients void promptly and without difficulty after operation; others may require catheterization at intervals for eight to twelve days after operation. In general, patients who are allowed out of bed promptly will recover urinary control more quickly, although this is not invariably true.

When the patient is unable to void and requires catheterization on more than three successive occasions, it is advisable to insert a retention bladder catheter. The catheter is removed after several days; if the patient then voids spontaneously several hours later, the bladder is catheterized at once to note the possible presence of residual urine. If inability to void persists or a significant amount of residual urine is present, the retention catheter is replaced for a day or two. As a rule, occasional catheterization will be needed after the ordinary vaginal plastic repair of cystocele or urethrocele, but a retention catheter will not be required unless the bladder has been injured accidentally



during operation. A retention catheter, although not strictly necessary, may be used as a routine for several days following operations for prolapse, including vaginal hysterectomy, the Wertheim-Watkins interposition operation, and the Manchester-Fothergill operation, as well as following repair of an extensive cystocele or a third degree perineal laceration. When such a catheter is used, it should be taped to the thigh and connected to a rubber tube passing beneath the thigh and into a bedside drainage bottle (Fig. 19). When catheterization is repeated frequently, or residual urine is present, or a retention catheter is used, prophylactic doses of sulfadiazine or sulfacetimide are administered.

*Diet in the average case is amplified as rapidly as possible.* A surgical liquid diet is given after postanesthetic nausea disappears, a soft diet is begun on the third day, and a full diet is allowed as soon as the patient desires it. Infusions of protein hydrolysate and high protein dietary supplements orally or by stomach tube are given as indicated in severely malnourished or seriously ill patients. After repair of a rectovaginal fistula or of a complete tear of the anal sphincter, a nonresidue liquid or soft diet is supplied for ten days; during this time the sulfasuxidine or sulfathalidine begun before operation is continued in half or full dosage and an opiate (for example, paregoric in small doses twice daily) is given to maintain constipation. When ten to twelve days have passed, a mild saline laxative such as milk of magnesia (15 c.c. twice daily) is given until a soft stool is obtained. A liquid stool is undesirable; tenesmus may result, with excessive strain on the area of operative repair.

The time for removal of drains varies according to the purpose served by the drain. The vaginal sponge inserted following dilatation and curettage of the uterus is removed after twenty-four hours; cigarette drains are withdrawn from the prevesical space of Retzius after forty-eight hours, and rubber drains used in the superficial layers of the abdominal incision also are removed after two days. When vaginal drainage is used following abdominal total hysterectomy, the cigarette drain is withdrawn in four to six days according to the preference of the surgeon. It is a worth-while precaution to note on the patient's chart the number, type, and location of drains used at operation and the date when each is removed. The patient should always

be examined before discharge from the hospital for the possible presence of overlooked unremoved drains, especially in the vaginal tract.

Pain and discomfort following perineal operations are decreased by local use of a heat lamp for one hour three times daily. With improvement in quality and strength of suture material in recent years, silk, cotton, or fine (00 to 0000) chromic catgut can be used for vaginal plastic procedures, the post-operative discomfort being considerably diminished in severity and duration by the finer suture material. If nonabsorbable sutures are used, they are removed after twelve days; catgut sutures are permitted to absorb spontaneously. No vaginal drains or sponges are used following colporrhaphy, since bleeding is slight; moreover, gauze drains are likely to become entangled in projecting suture ends upon withdrawal. Vulvar pads also are unnecessary in these cases; they are as likely to retain infected material in contact with the suture lines as to prevent soiling by unsterile surfaces and objects. The vulva and perineum are irrigated with potassium permanganate (1:5,000), boric acid (4 per cent), or aqueous Zephiran (1:2,000) solution following urination or defecation on each occasion, and the heat lamp is used to dry the area thoroughly. The use of douches is optional; if administered, douches should be given gently with a small soft rubber catheter. In some cases the administration of vaginal suppositories of estrogenic substance, instituted pre-operatively to encourage increased vascularity of the vaginal mucosa, may be continued after operation until full healing has occurred.

### Postoperative Complications

Postoperative hemorrhage is more common following vaginal operations than following laparotomy. Hemorrhage appears primarily within six to fourteen hours after operation or secondarily after ten to fourteen days. For treatment the vagina is packed, the foot of the bed is elevated eighteen inches, morphine is given hypodermically in full dosage or slowly intravenously in half dosage, and a blood transfusion is administered promptly. If hypoprothrombinemia is present or even suspected, a soluble menadione derivative is given parenterally (2 to 5 mg.). Supportive measures are sufficient to stop the

bleeding in most cases, although it is occasionally necessary to return the patient to the operating room for control of bleeding by suture.

Use of anticoagulants such as heparin and dicumarol in prophylaxis of venous thrombosis occasionally may result in seepage of blood, particularly into areas of vaginal plastic repair. When anticoagulant therapy is planned, it should not be begun until at least six hours following operation in order to permit secure clot formation in the divided vessels. Continued bleeding due to the effects of anticoagulants can be stopped promptly by a transfusion of fresh whole blood (p. 392); further use of such drugs is postponed for at least twenty-four hours. Small hematomas will absorb spontaneously over a period of several weeks; large hematomas are evacuated under anesthesia in the operating room.

Pulmonary atelectasis and secondary bronchopneumonia are most common in elderly patients, in whom decreased vital capacity, chronic bronchopulmonary infection, pulmonary fibrosis, and anemia are likely to be present. Prophylaxis by administration of carbon dioxide inhalations, frequent changes of position, deep-breathing exercises, vigorous movements of the legs, and early ambulation will be sufficient in most cases. If evidence of atelectasis should appear, treatment is instituted promptly by carbon dioxide inhalations, induced coughing, tracheobronchial suction if necessary, and administration of penicillin or sulfadiazine in full dosage. Pulmonary atelectasis is especially dangerous in aged patients, in whom a fatal secondary bronchopneumonia can speedily develop.

Phlebothrombosis, thrombophlebitis, and pulmonary embolism have always been relatively frequent in gynecologic patients. For early recognition of venous thrombosis, the legs and feet should be examined daily as a routine and the chart inspected for unexplained minor elevations of temperature and pulse rate. It is highly important to insist on vigorous exercising movements of the feet and legs at frequent intervals throughout each day, beginning immediately after recovery from anesthesia. \*All the well-recognized measures of prophylaxis against venous clot formation should be taken as a routine; in occasional cases prophylaxis with a full course of heparin or dicumarol is

advisable. In many clinics which report a high incidence of postoperative venous thrombosis, bilateral ligation of the superficial femoral veins is performed at the time of operation in aged patients, in patients with cardiac disease, and in patients with large pelvic tumors. Collins and associates<sup>4</sup> have pointed out that swelling of one or both legs observed before operation in patients with pelvic tumors may be due not to venous obstruction by direct pressure but to fully developed preoperative phlebothrombosis. These authors report that five fatal emboli in a series of twelve deaths from pulmonary embolism occurred preoperatively in patients being prepared for removal of pelvic tumors presumably causing peripheral edema by pressure.

Perforation of the uterus during curettage is not an uncommon occurrence. If the uterus is uninfected, the damage is minimal, and the accident is recognized at once, a sterile sponge is inserted into the vagina and the patient is returned to her room. If the perforation is large, or the curette has passed through the uterine wall more than once, or there is a possibility that damage to the intestine has occurred, laparotomy is performed immediately. When perforation occurs during removal of infected clots or retained products of conception following septic abortion, hysterectomy is done at once. Since curettage is not often done for this indication, the accident is correspondingly uncommon. In any case penicillin and sulfadiazine are administered in full therapeutic dosage for a week or more, the initial dose being given in the operating room without loss of time.

Fecal fistula may develop following separation of inflammatory adhesions between the small or large bowel and the pelvic organs. Such diseases as pelvic inflammatory disease, tubo-ovarian abscess, tuberculosis of the genital tract, endometriosis, carcinoma, or degenerating fibromyomas are likely to cause such dense fixation of the diseased organs to adjacent structures that clean separation without damage may be impossible. If the bowel wall is traumatized during operation, the defect is repaired by suture or resection or is exteriorized. Extensive areas of damage in the sigmoid or rectosigmoid that cannot be exteriorized following repair should be protected by temporary establishment of a complete transverse colostomy. As a prophylactic measure it may be advisable to leave two cigarette drains down to the pelvic cavity at operation following injury to the bowel with

gross peritoneal contamination; such drains are brought along the lateral wall of the abdominal cavity and out through a small lateral abdominal stab wound, to avoid contact with the small intestine. Care is taken not to place the ends of the drains in contact with bowel or with suture lines.

An unrecognized or insufficiently repaired area of damage to the bowel is likely to cause postoperative peritonitis or fecal fistula. As the intestinal leakage accumulates and bacterial growth takes place, a spreading abscess develops and drains into the pelvic cavity, the general peritoneal cavity, or the abdominal incision. Evacuation of the abscess may be followed either by spontaneous healing or by a fecal fistula. In either case an extensive wound infection of a mixed type will develop, with drainage of purulent material having a fecal odor. Wound infection due to colon organisms can be differentiated from a small fecal fistula by oral administration of methylene blue or charcoal; larger fistulas can be identified at once by expulsion of intestinal gas and feces. Administration of sulfasuxidine or sulfathalidine, as well as penicillin or sulfadiazine, is begun at once in all cases. Streptomycin is given if the general toxic reaction is severe or if spreading peritonitis or septicemia develop. When external drainage is not fully effective or when the fecal discharge is copious, a complete transverse colostomy should be performed promptly. Most fecal fistulas occurring secondarily to gynecologic operations will close spontaneously in time; in any case surgical repair should not be attempted in less than six to twelve months.

Although intestinal fistulas developing within the peritoneal cavity are the most dangerous to life, other types of fistulas may appear and cause considerable annoyance. Vesicovaginal fistula may occur following anterior vaginal plastic operations or total hysterectomy, rectovaginal fistula may complicate posterior colporrhaphy, and rectovaginal or rectocervical fistula occasionally may develop after injury to the rectum during hysterectomy.

The ureter may be crushed or ligated accidentally in the course of hysterectomy (especially total) or removal of a deep intraligamentary tumor; it is advisable to place a catheter in each ureter before radical total hysterectomy or removal of a tumor which has become fixed in the pelvis. Identification of the course of the ureter by dissection during operation is not always an

entirely harmless procedure; much of the ureteral blood supply may be stripped from its walls, with subsequent sloughing and fistula formation. Occasionally, accidental ligation of a ureter will be followed by atrophy of the kidney without production of symptoms; in most cases pain develops in the region of the obstructed kidney and a palpable tender mass appears. Retention of urine in the kidney pelvis under pressure will produce pyelitis if bacteria are present; the usual symptoms of upper urinary tract infection appear but fail to respond to treatment. Symptoms of intractable pyelitis, with or without pyuria, occurring in the early postoperative period should always suggest the possibility of ureteral block, whether due to a ligature or to some other cause. Ureteral catheterization is attempted as soon as intensive medical therapy proves ineffective; if the catheter cannot be passed beyond the obstruction, a temporary nephrostomy may be necessary. It is not advisable to perform a second laparotomy for repair of the injured ureter until at least six weeks have passed, in order to allow the patient to regain sufficient strength to withstand the possibly prolonged operation of ureteral repair and to permit the inflammatory reaction about the damaged ureter to subside. Frequently, spontaneous cessation of urinary leakage will occur as a result either of ureteral occlusion or, less commonly, of healing.

Crushing of the ureter during hysterectomy may cause pyelitis due to obstruction, followed by leakage of urine through the vagina as sloughing of the damaged segment occurs. Free drainage of urine through the fistula is followed by subsidence of the pyelitis, which may recur if the fistulous tract becomes blocked for any reason. Differentiation between ureterovaginal and vesicovaginal fistula can be made most simply by catheterization of the bladder and introduction of a sterile dilute solution of methylene blue. If the vaginal drainage is clear, the fistula is ureteral; if colored blue, the urine is leaking from a vesical fistula. Ureteral catheterization and intravenous pyelography will permit accurate localization of the ureteral defect. As in the case of ureteral ligation, temporary nephrostomy is advisable if drainage of urine is obstructed and untoward symptoms develop; if drainage is free, the patient is observed until healing occurs or conditions are optimal for corrective surgery.

Repair of vesicovaginal fistula is delayed for perhaps six months after development of the defect, the tissues must be firm, healthy, and normally vascular, with no remaining edema, infection, or inflammation. If the fistula recurs following operative repair, another similar interval of time should be allowed to pass before a second attempt at repair is made; operation through tissue which has not completely healed following the previous repair is almost certain to be unsuccessful again. Since each operative failure adds to the tissue damage, increases the extent of the fistula, and renders future surgery more difficult, repair should not be attempted until conditions are optimum for a successful result.

Both the patient and the surgeon are understandably anxious to secure closure of the fistula at the earliest possible moment because of the annoying or even incapacitating constant urinary leakage. Pads and tampons are of little help and a retention catheter is scarcely practical. An apparatus which may prove helpful has been suggested by Castallo<sup>4</sup>: a mushroom catheter is passed through a small hole in the center of a contraceptive vaginal diaphragm of the proper size and the catheter tip is cut off to leave a flange, which is cemented to the inside of the dome. With the apparatus in place, the catheter can be adjusted to drain into a baby-sized hot-water bottle strapped to the ambulatory patient's thigh, or into a bottle at the side of the bed. In any case, sitz baths are taken regularly and douches containing 45 c.c. of vinegar to 2 quarts of water are used frequently to keep the vagina and vulva clean of urinary sediment and crystals of urinary salts.

Operative repair is usually performed by the vaginal route. The most important consideration in postoperative care is maintenance of proper bladder drainage to avoid bladder distention and prevent leakage of urine through the sutured wound. The plan for securing postoperative bladder drainage advocated by TeLinde<sup>5</sup> is as follows: the patient is allowed up to void immediately after operation following simple repair of an uncomplicated vesicovaginal fistula; if this does not prove satisfactory, an indwelling urethral catheter is preferred to repeated catheterization. Following a difficult repair the patient is kept in bed for two weeks with an indwelling urethral catheter, as well as a mushroom catheter introduced into the bladder through a short

midline vaginal cystotomy incision performed at the time of operation. The point is made that a small elective cystotomy incision of this type, made through normal undamaged tissue, will heal spontaneously following removal of the catheter, its advantage is that it insures constant drainage of the bladder with the patient supine. Patency of the catheters is checked by injection of 5 to 10 c.c. of sterile normal salt solution daily. If the anterior vaginal wall is too scarred to permit cystotomy drainage, a suprapubic catheter is introduced at the time the fistula is repaired, to remain for two to three weeks.

### References

1. Falk, H. C., and Hochman, S.: Intestinal Injury and Fecal Fistula in Gynecological Surgery, *Am. J. Surg.* 70: 176, 1945.
2. Lash, A. F.: Surgical Geriatric Gynecology, *Am. J. Obst. & Gynec.* 53: 766, 1947.
3. Collins, C. G.: Cotton Sutures in Vaginal Plastic Operations About the Bladder and Urethra, *S. Clin. North America* 26: 1221, 1946.
4. Collins, C. G., Nelson, E. W., Jones, J. R., Weinstein, B. B., and Thomas E. P.: Ligation of the Vena Cava, *New Orleans M. & S. J.* 99: 488, 1947.
5. Castallo, M. A.: Apparatus for the Control of Vaginal Urinary Incontinence Due to Fistulas, *J. A. M. A.* 133: 244, 1947.
6. TeLinde, R. W.: Surgical Cure of Urinary Incontinence in Women, *Ann. Surg.* 126: 64, 1947.



## APPENDIX

TABLE VI. BLOOD CHEMISTRY VALUES

DETERMINATION	NORMAL VALUE	HIGH VALUES FOUND	LOW VALUES FOUND
Amylase (serum)	15-180 Somogyi units per 100 c.c.	Acute pancreatitis (early)	Scurvy, vitamin deficiency states; malnutrition
Ascorbic acid (plasma)	0.5-1.0 mg. per 100 c.c.		
Bilirubin (serum)	Direct. 0.4 mg. per 100 c.c. Indirect (total): 0.7 mg. per 100 c.c.	Obstructive jaundice, hepatic disease (direct); hemolytic jaundice (indirect)	
Calcium (serum)	9.0-10.5 mg. per 100 c.c.	Hypoparathyroidism	Hypoparathyroidism, rickets; nephrosis
Carbon-dioxide combining power (serum)	55-75 volumes per cent	Alkalosis	Acidosis; diabetes; nephritis; starvation, dehydration; diarrhea
Chloride (as sodium chloride)	Whole blood: 450-521 mg. per 100 c.c. Plasma: 550-650 mg. per 100 c.c.	Nephritis, cardiac disease; anemia	Pneumonia; diabetes; vomiting; starvation; gastrointestinal tract obstruction

Cholesterol (serum)	150-200 mg. per 100 c.c.	Obstructive jaundice; diabetes; nephritis; hypothyroidism; pregnancy	Pernicious anemia; cachexia of malignancy; hyperthyroidism; severe hepatic disease
Cholesterol esters (serum)	90-130 mg. per 100 c.c.		
Glucose (serum)	80-110 mg. per 100 c.c.	Diabetes; advanced nephritis	Hyperinsulinism
Iodine (as thyroid hormone)	0.004-0.008 mg. per 100 c.c.	Hyperthyroidism	Hypothyroidism
Nonprotein nitrogen (serum)	25-35 mg. per 100 c.c.	Renal insufficiency; urinary retention; intestinal obstruction; dehydration; fever; shock, vomiting	Acute hepatic failure
Urea nitrogen (serum)	10-15 mg per 100 c.c.	Parallels nonprotein nitrogen	
Phosphatase, acid (serum)	0.5-3.0 King and Armstrong units	Osteous metastases in carcinoma of prostate	
Phosphatase, alkaline (serum)	2-4.5 Bodansky units or 5-13 King and Armstrong units	Disease of bone; obstructive jaundice, hepatic carcinoma	Anemia
Phosphorus, inorganic (serum)	3-4.5 mg. per 100 c.c.	Parathyroid tetany; nephritis; major fractures	Hyperparathyroidism; rickets

TABLE VI. BLOOD CHEMISTRY VALUES—CONT'D

DETERMINATION	NORMAL VALUE	HIGH VALUES FOUND	LOW VALUES FOUND
Proteins (plasma) Total	6.0-8.0 Gm. per 100 c.c.	Shock not due to blood loss; burns; dehydration	Shock due to blood or plasma loss; nephrosis, nephritis; starvation; cardiac decompensation
Fibrinogen	0.2-0.8 Gm. per 100 c.c.	Pregnancy; pneumonia; pyogenic infections	Typhoid fever; acute yellow atrophy of the liver
Albumin	4.5-5.5 Gm. per 100 c.c.	Same as total protein	
Globulin	1.5-3.0 Gm. per 100 c.c.		
Uric acid (serum)	3.0-5.0 mg. per 100 c.c.	Renal insufficiency; gout; cardiac decompensation	
Creatinine (serum)	1.0-2.0 mg. per 100 c.c.	Terminal nephritis	

### Diet Lists

Most hospitals have a routine diet plan which is consistently followed for each general type of surgical patient, with variations to suit individual needs. The simpler diets are low in caloric value and, if maintained over relatively long periods of time, must be supplemented by intermediate nourishments or by parenteral administration of nutritive fluids. In most cases progression from the simple diets to the more substantial ones can be made rapidly, although the rate of progress must be decided individually for each patient.

Typical foods included in special diets are:

#### I. Surgical Liquid Diet

Consommé, broth  
Ginger ale, Coca-Cola  
Tea, coffee (weak)

#### II. Semisolid Diet

*Add:*

Cooked cereal  
Buttered toast  
Cream soups  
Soft-cooked or poached egg  
Milk, cream, fruit juices  
Custard, ice cream, Jello

#### III. Surgical Soft Diet

*Add:*

Cooked fruit, without skins  
Cereal, except whole wheat or bran  
Eggs, poached, soft-cooked, omelet (baked)  
Potato, any form except fried  
Bread, white (plain or toasted)  
Vegetables, puréed (carrots, peas, lima beans, squash, beets, spinach, cauliflower)  
Prepared foods (macaroni, spaghetti, rice, hominy, grits)  
Desserts (Jello, custards, simple puddings, ice cream, sherbets)

#### IV. Low-Residue Solid Diet

Same as surgical soft diet, with the addition of:

Meat (chicken, fish, lamb, roast beef, sweetbreads)

*Avoid especially:*

All coarse cereals, vegetables, bread, and fruits  
Raw fruits and vegetables  
Pork, veal, preserved fish and meats  
Fried or fatty food  
Spices and sauces  
Pastry

### V. Regular Diet

All foods usually taken by the patient

Diet for colostomy patients as outlined by Cattell.\*<sup>1</sup>

"Colostomy Diet No. 1—Used in hospital while first gaining control and at any time later when loose movements occur.

"*Breakfast*: Large portion of cream of wheat with boiled milk, sugar if desired; 2 hard-boiled eggs, dry toast; 1 glass of boiled milk.

"*Lunch*: Creamed soups (creamed lettuce soup three or four times a week); creamed fish or meat; baked or mashed potato, boiled rice or custard.

"*Dinner*: Meat or fish, creamed whenever possible, escalloped vegetable—no spinach or carrots; soft pudding, custard or junket.

"Colostomy Diet No. 2—Used after gaining control in the hospital (two weeks) and continued for two months at home.

Cream of wheat, puffed wheat or puffed rice.

Eggs, boiled, poached, baked or scrambled.

Oven-broiled bacon

White bread, plain or toasted.

Plain white crackers or saltines

Butter, cheese, milk, tea, coffee, cocoa.

Boiled rice. Baked macaroni or spaghetti.

Baked custards.

Soups of all kinds except tomato or corn.

Potato, baked, mashed, or riced.

Roast beef, lamb, or chicken.

Broiled steak or lamb chop.

Fish, broiled, boiled, creamed.

Sponge or angel cake.

"Colostomy Diet No. 3—Added to No. 2 after two months if control is still effective.

Raw lettuce and celery.

Cooked string beans, peas, carrots, beets, winter squash, cauliflower, asparagus.

Cooked fruits.

Orange juice."

### Preparation for X-Ray Studies

If the patient is to have a gall bladder visualization, gastrointestinal series, and barium enema, the examinations should be performed in that order, so that radiopaque material remaining from a previous study will not interfere with the visualizations subsequently desired.

\*From Cattell: S. Clin. North America 18: 755, 1935. W. B. Saunders Co

1. **Cholecystography.**—The gall bladder dye is administered the day before the roentgenograms are taken in the following manner: Immediately after the noon meal, which should be fat free, with no meat, butter, or fatty food, the patient is given 4.0 Gm. of tetraiodophenolphthalein in grape juice, and thirty minutes later, 6 c.c. of paregoric. After an evening meal of a similar type, the doses of gall bladder dye and of paregoric are repeated according to the same plan. Nothing else but water is permitted by mouth until after the first roentgenograms are taken. The patient receives a tap water enema the following morning, after which a roentgenogram of the gall bladder region is made. Pituitrin (1.0 c.c. hypodermically) may be used if desired to reinforce the effect of the enema in clearing the colon of gas and solid contents, but use of the drug is inadvisable in pregnant women and in hypertensive individuals. If the gall bladder is not visualized by x-ray at this time, the test should be repeated the following day. After a satisfactory roentgenogram has been taken, the patient receives a meal containing a large proportion of fat, and another x-ray is made an hour later.

The gall bladder dye is bitter and may cause severe nausea. If the drug is vomited, a fresh dose should be given as soon as the patient recovers. Tetraiodophenolphthalein is not given in the presence of obstructive jaundice or acute biliary tract disease or to patients who have deficient kidney function.

Other organic iodine compounds which cause less nausea and vomiting than the phenolphthalein derivatives are available for gall bladder visualization. Priodax, for example, is given during or after the evening meal in a dose of six 0.5 Gm. tablets, taken singly at five-minute intervals with water, a full glass of water being taken with the last tablet. Nothing except water and fruit juice is permitted by mouth from that time until the first x-ray has been made the following morning. An enema may be given two hours before x-ray, if desired. A fatty meal is supplied, and a second x-ray is taken an hour later to determine the degree of gall bladder emptying.

2. **Gastrointestinal Series.**—No preparation is required except that the patient should not be given any cathartics during the preceding twenty-four hours and no food or water after midnight. Fluoroscopy is performed in the morning as the pa-

tient swallows the barium meal, and roentgenograms of the upper intestinal tract are made immediately afterward. Another plate is taken six hours later for evidence of gastric retention; nothing by mouth is permitted until after this picture has been made. Ordinary diet is then resumed. A final x-ray picture is usually taken the next morning to discover any evidence of retention of barium in the stomach or small intestine.

3. **Barium Enema.**—The patient receives a cleansing tap water enema the night before the roentgenologic examination and another four hours before. If there is any evidence of an obstructive or inflammatory lesion of the bowel, no cathartic is given. If not contraindicated, castor oil, 30 c.c. (1 ounce), will insure complete clearing of the colon. Barium remaining in the bowel after x-ray is washed out with a tap water enema.

### Oxygen Administration

**Indications.**—Decrease in the hemoglobin content of the blood, as in secondary (iron deficiency) anemia, or decrease in the hemoglobin available for oxygenation, as in sulfanilamide poisoning, is compensated to some extent by an increase in circulatory rate and perhaps an increase in respiratory rate. This mechanism, however, may prove inadequate under the added burden of a surgical operation, and anoxemia will then develop. Although clinical cyanosis is a definite indication of anoxemia, it is not always present in such cases; the oxygen content of the blood may be low enough to cause a dangerous tissue anoxia even if the hemoglobin content of the blood is too low to produce the characteristic blue coloring. It is often advisable therefore to administer oxygen to anemic patients for a day or two following major surgery in order to reduce the danger of surgical shock.

Shock is characterized by a decrease in circulating blood volume and a retardation of blood flow, with consequent anoxemia. As a result of the decreased rate of blood flow, the capillaries become anoxic and dilated. As loss of plasma continues, progressive hemoconcentration develops, the atonic capillaries filling with sluggishly moving corpuscles. The increased viscosity and decreased volume of the blood cause still further retardation of circulatory rate, with accentuation of



anoxemia. Proper therapy of shock includes restoration of blood volume by transfusion of whole blood or plasma, institution of the accepted symptomatic measures, and elevation of the oxygen content of the blood and tissues by administration of pure (100 per cent) oxygen. It should be noted, however, that clinical improvement attributable to the use of oxygen in shock is generally slight, even though the theoretic basis for its administration is sound,

Oxygen in concentrations of 50 per cent or more is of value in the management of patients with cardiac or pulmonary disease during the early postoperative period. Pure oxygen by inhalation is used also for the severe dyspnea accompanying pulmonary embolism and for the prevention and treatment of thyroid crisis. Oxygen is of some value in the care of patients who exhibit depression of liver function. Existing hepatic damage is increased by even slight degrees of anoxemia, and the administration of oxygen may prevent further injury. Patients who have liver damage should be given oxygen in high concentration not only during operation, but also during the immediate postoperative period, to be continued as long as necessary. Oxygen is of especial value in the care of pulmonary complications following operation. Pulmonary atelectasis is best treated by postural changes, inhalations of carbon dioxide, and tracheobronchial aspiration, but oxygen can be given with profit for several hours following removal of the mucous plug. Secondary bronchopneumonia demands the administration of oxygen as a therapeutic adjunct.

Pulmonary edema, which may develop suddenly following operation in a patient with disease of the heart or lungs, is one of the most dangerous of the postoperative complications. The unfortunate patient literally drowns as a result of the rapid exudation of serum across the congested and swollen anoxic alveolar walls into the alveoli. Ordinary therapeutic measures, even administration of pure oxygen, are generally fruitless, since the inspired air is unable to enter the fluid-filled alveoli and the patient's increased respiratory efforts themselves add to the oxygen lack. The only treatment which offers a hope of success is the administration of 100 per cent oxygen under positive pressure,<sup>2</sup> either by a resuscitation apparatus or by an anesthetic machine. A gentle pressure, not to exceed 6 cm. of water, is applied inter-

mittently during the patient's inspiratory efforts until the pulmonary congestion has decreased enough to allow proper aeration by spontaneous breathing. The administration of 100 per cent oxygen is then continued for several hours, until clinical signs of pulmonary congestion have disappeared.

The administration of 100 per cent oxygen, as an adjunct to suction drainage, has been found to be helpful in the relief of intestinal distention<sup>1</sup> in patients with severe postoperative "gas pains" or with actual obstruction. The intestinal gas responsible for distention is largely nitrogen, since it is composed chiefly of swallowed air. Inhalation of pure oxygen results in the replacement of the mixture of nitrogen and oxygen in the pulmonary alveoli with oxygen alone. When the partial pressure of alveolar nitrogen is thus reduced, more of the nitrogen dissolved in the circulating blood will diffuse out into the alveoli and be exhaled. The resulting decrease in partial pressure of nitrogen in the plasma permits some of the nitrogen contained in the distended bowel to be absorbed into the blood stream, and this dissolved gas is carried out through the lungs in its turn. The effectiveness of oxygen therapy is increased if the patient receives the gas through an apparatus which covers both the mouth and the nose, so that no more air will be swallowed until after the existing distention has been relieved. Improvement, when it occurs, is ordinarily noted within several hours but must not be permitted to interfere with the performance of any necessary surgery for relief of the intestinal obstruction.

Headache due to retained intracranial air following encephalography sometimes can be relieved by administration of pure oxygen for several hours; the effectiveness of oxygen here is based also on the principle of nitrogen absorption. Inhalation of 100 per cent oxygen can be used in treatment of headaches following spinal puncture and spinal anesthesia, and in the latter case serves also to counteract the tendency to anoxemia and generalized tissue anoxia consequent to the sustained drop in blood pressure. Pure oxygen has been used in the treatment of migraine but without notable success.

Administration of oxygen by means of a *tent* has been well standardized; concentrations of oxygen up to 50 or 55 per cent can be maintained. The tent is bulky, complicated, and expensive, requiring the care of a special attendant, but the

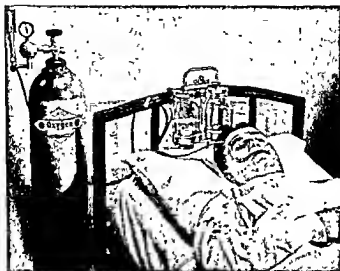


Fig. 74—Oxygen administration by nasal catheter (Courtesy The Ohio Chemical & Mfg Co)

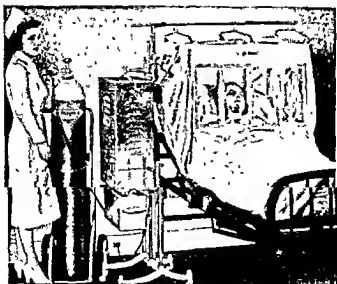


Fig. 75—Oxygen administration by tent (Courtesy The Ohio Chemical & Mfg. Co)

atmosphere within it is cool and comfortable. Because of the possibility of leaks, the oxygen content within the tent should be tested at least twice each day to make sure that the proper concentration is maintained. The tent should have a minimum

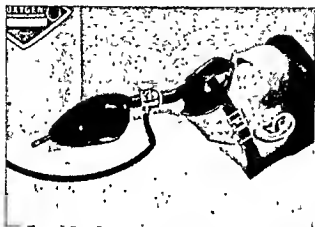


Fig. 76.—Oxygen inhalation apparatus, oronasal mask (From Boothby, Mayo, and Lovelace J A M A 113: 480, 1939)

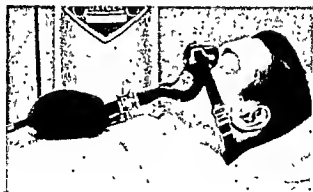


Fig. 77.—Oxygen inhalation apparatus, nasal mask (From Boothby, Mayo, and Lovelace J A M A 113: 480, 1939)

capacity of eight cubic feet; temperature should be kept within a range of 60 to 68° F. and relative humidity at 40 to 60 per cent. Oxygen flowing at a constant rate of 8 liters per minute and cooled by circulation directly through an icebox will maintain

the oxygen content within the tent at approximately 50 per cent and the temperature and humidity at the proper levels. The blower should be stopped before the icebox is opened to refill with ice. Following loss of oxygen from the tent incidental to nursing care of the patient or of the apparatus, the rate of inflow is increased for a short time to restore the proper oxygen concentration.

When an *intranasal catheter* (12 French) is used to administer oxygen, the tube is passed into the nose for approximately three inches and is taped to the nose and forehead. Oxygen is

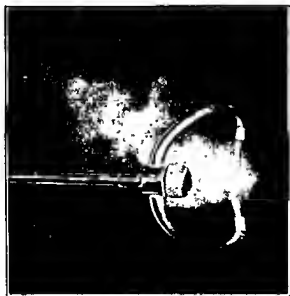


Fig. 78.—Mask for oxygen administration. (From Lombard and Nelson, *J. Lab. & Clin. Med.* 24: 725, 1939.)

given continuously at the rate of 5 to 7 liters per minute and should be bubbled through a closed container of water attached to the tank, to prevent drying of the patient's pharynx. Concentrations of oxygen up to 35 to 40 per cent in the alveolar air can be attained by this method.

The B.L.B. mask<sup>4</sup> described by Boothby and associates (Figs. 76 and 77) consists of three parts: a mask of either the nasal or the oronasal type, a connecting-regulating device with a series of air vents to permit regulation of the concentration of oxygen administered, and a reservoir bag. The desired per-

centage of oxygen is obtained by adjusting the flow from the tank and opening the requisite number of air holes in the regulating valve on the mask connection. As the vents are successively closed and the flow from the oxygen tank is increased,



Fig. 70 —Mask for oxygen administration. (From Lombard and Nelson  
*J. Lab. & Clin. Med.* 23: 725, 1939)

the percentage of oxygen inspired rises, and, as more air holes are opened, more air is inspired from the outside and less from the bag. To supply 100 per cent oxygen, all the air vents are closed and the flow of oxygen is increased. Oxygen must flow rapidly enough to fill the bag so that the patient will not empty the reservoir before his inspiration is completed, or a feeling of suffocation will result. A flow of 6 to 8 liters per minute is usually sufficient. If a concentration of 50 to 60 per cent oxygen is desired, the rate of flow from the tank is set at 4 liters per minute

and two air holes are opened, so that after the partially filled bag is emptied of its oxygen, continuance of inspiration will result in the inhalation of outside air.

Pure oxygen may be given continuously for as long as eight hours in each twenty-four, but the concentration should be decreased after that time. The apparatus should be removed and the patient's face washed and powdered every two hours. Oxygen therapy by mask should never be begun until after postanesthetic nausea and vomiting has ceased and the patient has recovered completely from the anesthetic.

Another simple apparatus for the administration of oxygen is the inhaler described by Lombard and Nelson<sup>5</sup> (Figs. 78 and 79). The apparatus consists of a transparent mask of cellulose acetate containing a Y-shaped metal tube, from each end of which a stream of oxygen flows, the velocity of each jet of gas neutralizing the other. The mask is made in two jointed sections so that the patient can be fed simply by raising the lower section. Before reaching the mask, the gas is bubbled through a container of water attached to the tank. Alveolar oxygen concentrations attained by a flow of 4.5 to 7 liters per minute are stated to be the same as those afforded by a tent containing 40 to 50 per cent of oxygen. Higher percentages of oxygen cannot be attained by this apparatus.

### References

1. Cattell, R. B.: Symposium on Cancer: Management of Colostomy, *S. Clin. North America* 18: 755, 1938.
2. Boothby, W. M., Mayo, C. W., and Lovelace, W. R., II: The Use of Oxygen and Oxygen-Helium, With Special Reference to Surgery, *S. Clin. North America* 20: 1107, 1940.
3. Fine, J., Hermanson, L., and Frehling, S.: Further Clinical Experiences With 95 Per Cent Oxygen for Absorption of Air From the Body Tissues, *Ann. Surg.* 107: 1, 1938.
4. Boothby, W. M., Mayo, C. W., and Lovelace, W. R., II: One Hundred Per Cent Oxygen; Indications for Its Use and Methods of Its Administration, *J. A. M. A.* 113: 477, 1939.
5. Lombard, C. F., and Nelson, C.: New Apparatus for Oxygen Therapy, *J. Lab. & Clin. Med.* 24: 724, 1939.

### Infusions and Transfusions

Because so many hospitals employ commercially prepared and sterilized equipment for administration of infusions and for collection and administration of transfusions, descriptions of several of the more widely used methods are given below. In addition to the specific types of equipment described, others of equal excellence and differing only slightly in methods of use are available from other manufacturers. The information and illustrations were supplied by the respective manufacturers.

**Vacoliter Solution Administration Technique (Baxter).**—Solutions for intravenous administration, prepared and sterilized by the manufacturer, are supplied in vacuum flasks (Vacoliter) of various sizes. The contents of the flask are identified both by the label and by the marking on a metal disk on the cap.

Fig. 80

Fig. 81

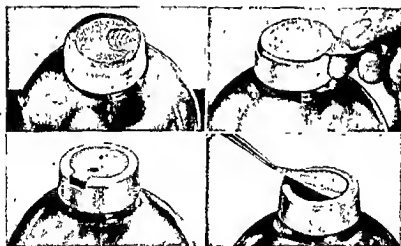


Fig. 82.

Fig. 83.

Fig. 80.—Vacoliter flask. To open, the metal tab is pulled downward. (Courtesy Baxter Laboratories, Inc., Glenview, Ill.)

Fig. 81.—Vacoliter flask. The metal cap is pried off with the metal tab. (Courtesy Baxter Laboratories, Inc., Glenview, Ill.)

Fig. 82.—Vacoliter flask. The stopper is protected by a rubber disk, which should be depressed in two spots by the vacuum in the flask. (Courtesy Baxter Laboratories, Inc., Glenview, Ill.)

Fig. 83.—Vacoliter flask. The rubber disk is pulled off with sterile forceps. (Courtesy Baxter Laboratories, Inc., Glenview, Ill.)



To prepare for administration, the outer seal is removed by lifting the corrugated metal tab (Fig. 80) and pulling outward and downward; the tab should not be twisted. The seal is removed, exposing the metal cap. This cap is lifted off (Fig. 81), exposing a thin rubber sheet or disk covering the stopper of the flask (Fig. 82). The rubber disk should appear to be depressed into the two holes of the stopper beneath, indicating that the vacuum within the bottle is intact and therefore that the contents are sterile. Absence of the depressions in the rubber disk would signify that the vacuum had been broken; under such circumstances the solution should not be used. The bottle is inverted once to moisten the inside of the stopper, following which the rubber disk is pulled off with sterile forceps (Fig. 83).

There are two holes in the rubber stopper, one connected to a glass tube within the flask and the other free, with no connection. The end of a sterile connecting tube or of a Vacodrip, as illustrated, is introduced through the free hole in the stopper (Fig. 84). A screw clamp or shut-off clamp is placed several inches below the drip connection and is closed, after which the bottle is inverted and hung on an infusion stand. The end of



Fig. 84.—Drip tube is introduced through the stopper. (Courtesy Baxt Laboratories, Inc., Glenview, Ill.)

two rubber disks covering the stopper of the Transfuso-Vac; the first is removed with sterile forceps at this time, exposing the sterile surface of the second disk. The second disk is not removed but is allowed to remain to protect the sterile rubber stopper until the transfusion is finally administered.

The valve is closed by turning the corrugated knob clockwise and the needle on the end of the valve is introduced through the rubber stopper (Fig. 87) at the point marked X. The valve must be checked again at this time to make sure it is closed; leakage of air through it will cause loss of the vacuum in the collecting bottle.



Fig. 87.—Transfuso-Vac, assembling the collecting set. (Courtesy Baxter Laboratories, Inc., Glenview, Ill.)

The venipuncture needle is inserted into the donor's selected vein according to the usual technique (p. 177). The valve is opened slowly by turning the knob in a counterclockwise direction (Fig. 88) and blood should flow immediately into the flask. If no blood is obtained, the position of the needle in the vein

should be checked. The speed of collection can be regulated as desired by turning the valve knob in the proper direction. Blood should flow in a steady stream, but if too rapid aspiration is attempted the vein may collapse. The donor is asked to open and close his fist rhythmically to increase the rate of venous flow. During collection of the blood and for several minutes thereafter the flask is rotated gently to insure proper mixing of blood and anticoagulant. When enough blood has been obtained, the valve is closed before withdrawal of the needle, to prevent possible contamination of the contents of the flask by an inrush of air. The tourniquet is released, the needle is withdrawn from the donor's vein, and the valve is removed from the flask (Fig. 89). As a rule the amount of blood remaining in the tubing is sufficient for the required serologic specimens.

Blood collected in this manner may be given as a transfusion at once or it may be stored at an optimum temperature of 4° C., for as long as seven days before use. If the set has been assembled properly and the venipuncture performed carefully, there will be little likelihood of contamination of the blood. The vacuum still remaining in the bottle after collection of the blood is not released, in order to avoid introduction of unsterile air.

*For administration* the blood usually is given as it comes from the refrigerator, without being warmed. Rarely, the presence of a high titer of "cold agglutinins" in the recipient's serum (p. 168) makes it necessary to allow the blood to come at least to room temperature before administration. Under no circumstances, however, is it permissible to heat the blood before or during administration by placing it in water above body temperature or by applying hot-water bags to the flask or to the tubing. Reactions are more likely to follow administration of blood heated above body temperature than of blood chilled to refrigerator temperature.

The remaining rubber disk is removed from the top of the Transfuso-Vac and the top is cleaned with iodine and alcohol. The remaining partial vacuum is released by puncture of the larger indentation or hole in the stopper with an 18 gauge needle; the same needle then is introduced through the smaller indentation in the stopper (to which the glass tube within the flask is attached) to provide an air inlet during administration of the transfusion. The free end of the Filterdrip is pushed through

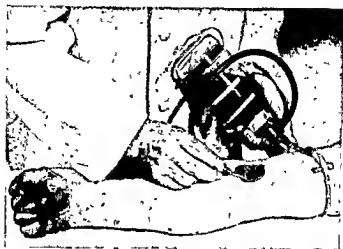


Fig 88—Rate of collection of blood controlled by adjusting valve  
(Courtesy Baxter Laboratories, Inc., Glenview, Ill.)



Fig 89—Blood remaining in the tubing is used for serologic specimens  
(Courtesy Baxter Laboratories, Inc., Glenview, Ill.)

the previously punctured large hole in the stopper and the tubing is filled with blood in the usual manner (Fig. 90). Finally, the bottle is hung from an infusion stand and the transfusion is administered.



Fig. 90.—Drip chamber and tubing are attached, after which the transfusion is administered. (Courtesy Baxter Laboratories, Inc., Glenview, Ill.)

The drip chamber (Filterdrip) in this apparatus contains a cylindrical filtering screen of fine-meshed stainless steel wire. The same drip chamber may be used without the filter for administration of infusions. Following completion of the transfusion, the drip chamber and filter should be taken apart, each section cleaned thoroughly, and reassembled before sterilization.

Blood that has been stored too long to use for transfusion (eight days) can be used as a source of plasma if contamination has not occurred and if there has been no hemolysis. During several days of undisturbed storage in a refrigerator, the cellular elements of the blood settle to the bottom of the flask so that a clear line of demarcation can be seen between cells and plasma.

Removal of plasma is accomplished by aspiration into a sterile vacuum bottle (Plasma-Vac), either large enough to serve as a pooling and storage container or small enough to accommodate only the plasma from a single flask of whole blood. The rubber disk is cut off the top of the flask of blood with sterile scissors, and the surface of the stopper is cleaned with iodine and alcohol. A sterile filter is connected through the large free hole in the stopper to eliminate the vacuum. It is

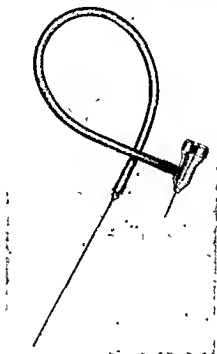


Fig. 91 —Valve and needle for aspiration of plasma from stored blood  
(Courtesy Baxter Laboratories, Inc., Glenview, Ill.)

important to avoid introducing the air filter through the smaller hole connecting with the glass tube in the flask; inrush of air bubbling through this tube would result in mixing of the layers of cells and plasma. When the vacuum has been neutralized the air filter is removed and is reinserted through the stopper at the point marked X. The plasma collection bottle (Plasma-Vac) is prepared, the aspirating valve is closed, and the valve needle

(Fig. 91) is inserted through the area marked X on the top of this bottle. The valve is allowed to remain closed and the long aspirating needle is inserted through the larger hole in the rubber stopper of the blood-containing flask. After the aspirating needle has been placed below the surface of the clean plasma, aspiration is accomplished slowly by cautious opening of the valve (Fig. 92). The needle must not be raised above the

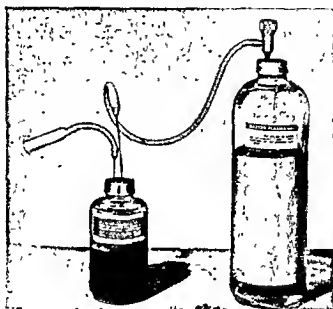


Fig. 92.—Pooling unit for collection of plasma from stored blood.  
(Courtesy Baxter Laboratories, Inc., Glenview, Ill.)

surface of the plasma or the vacuum will be lost; it must not be brought too close to the surface of the cell layer or mixing of blood and plasma will occur. When most of the plasma has been aspirated, the valve is closed. The aspirating needle is lifted *gently* above the surface of the remaining thin layer of plasma and is removed from the bottle of blood without contamination. If a pooling unit is being used (Fig. 92), the same procedure may be repeated as often as necessary to fill the flask. Chances of contamination increase with use; the same aspirating needle and valve should not be used more than six or eight times; if accidental contamination occurs it should be changed at once.

Cultures of the pooled plasma are taken and are incubated for ten days. Distribution of plasma into smaller units is done

Fig 93

Fig 94

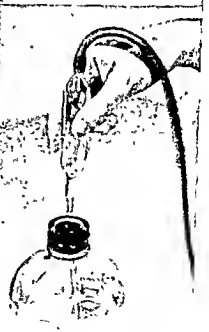


Fig 95

Fig 96

Fig. 93 —Soft flask. Metal seal is removed by puffing air. (Courtesy Cutter Laboratories, Berkeley, Calif.)

Fig. 94 —Cap is lifted off, revealing rubber liner. (Courtesy Cutter Laboratories, Berkeley, Calif.)

Fig. 95 —Rubber liner is removed; a hissing rush of air indicates that proper vacuum was present. (Courtesy Cutter Laboratories, Berkeley, Calif.)

Fig. 96 —Drip tube is inserted through larger hole in stopper. (Courtesy Cutter Laboratories, Berkeley, Calif.)



by a procedure the reverse of that described. It is customary to add a preservative, such as aqueous Merthiolate (final strength 1:10,000), for bacteriostasis.

**Saftiflask Solution Administration Technique (Cutter).—**Solutions for intravenous administration are prepared, sterilized, and sealed in vacuum flasks (Saftiflask) by the manufacturer. To prepare for use, the flask is inverted twice in order to moisten the inside of the stopper, and the metal seal is removed by means of the tab on the side of the cap (Fig. 93). The cap is lifted off (Fig. 94), revealing a rubber liner covering

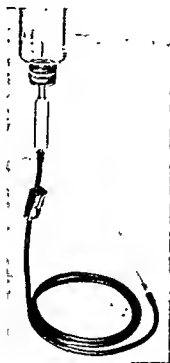


Fig. 97.—Rate of administration of infusion is adjusted by roller clamp below drip chamber. (Courtesy Cutter Laboratories, Berkeley, Calif.)

the stopper. The liner is lifted and removed (Fig. 95), a hissing sound indicating the inrush of air consequent to release of the vacuum. If this sound is not noted, it is possible that the vacuum may have been lost previously; under these circumstances, the solution should not be used. A connecting tube (Cutter

"dripmeter" illustrated) is introduced into the larger or free hole in the rubber stopper (Fig. 96).

The next step is removal of air from the tubing. The flask is held in the inverted position with the adapter end at a higher level. The clamp below the drip chamber is released and the flask is raised slowly until the entire tubing and adapter are filled with fluid. The needle is attached, the bottle is suspended, and the venipuncture is performed in the usual manner. The rate of flow is adjusted by means of the roller clamp (Safticlamp) on the tubing (Fig. 97).

**Saftivalve Technique for Blood Collection and Transfusion (Cutter).—**A special vacuum bottle (Saftifuge) is supplied by the manufacturer. The flask contains the proper amount of anticoagulant (citrate) and is protected by a sealed metal cap. After the donor has been prepared for venipuncture, the flask is shaken sufficiently to coat the inside with citrate solution and the seal on top is removed by a pull on the tab. The metal cap is taken off and should be saved and replaced after the blood has been collected. Removal of the cap exposes the rubber stopper (Fig. 98), which is perforated incompletely by three holes, each plainly marked.

The valve (Saftivalve) is examined to check the position of the tubing, which should be directly beneath the wheel (Fig. 99). The clamp is closed by rolling the wheel down and the needle hub is secured tightly. Failure to observe these precautions will result in loss of the vacuum in the collecting flask. The grip lever is pulled down to a horizontal position and the valve needle is inserted through the stopper at the hole marked Diaphragm. When the needle has passed into the flask far enough to allow the metal ring on the valve to drop below the glass ridge on the neck of the flask, the grip lever is snapped to an upright position, locking the valve to the flask. The clamp wheel is examined to make sure it is still closed tightly.

Venipuncture is performed according to the usual technique and aspiration of blood is begun when the clamp wheel is opened slowly (Fig. 100). If flow of blood does not begin as soon as the wheel is turned, the valve should be closed again and the venipuncture checked. Speed of flow is regulated by the degree to which the valve is opened; usually blood is collected at a rate of from 75 to 125 c.c. per minute. During collection and for several



Fig. 98.—Saftifuge vacuum flask for collection and transfusion of blood. Rubber stopper is marked but is not completely perforated. (Courtesy Cutter Laboratories, Berkeley, Calif.)



Fig. 99.—Roller clamp is closed; valve needle is introduced through "diaphragm." (Courtesy Cutter Laboratories, Berkeley, Calif.)

minutes afterward the blood and the citrate solution are mixed by gentle agitation of the flask. When sufficient blood has been obtained, the clamp wheel is closed tightly, the tourniquet is released, and the needle is withdrawn from the vein. The grip lever is pulled down and the needle is withdrawn from the flask, in which the vacuum is retained. The blood remaining in the tubing is sufficient for serologic specimens. Finally, the top of the stopper is cleaned with an antiseptic, the metal cap is replaced as a protective cover, and the flask is stored in a refrigerator until use.

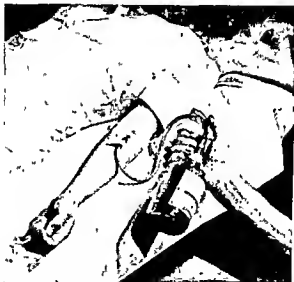


Fig. 100 — Rate of collection of blood controlled by roller valve  
(Courtesy Cutter Laboratories, Berkeley, Calif.)

When the transfusion is to be administered, the protective cap is removed, the top of the stopper is cleaned with an antiseptic, and the large indentation (marked Outlet) is punctured with a sterile venipuncture needle (19 to 21 gauge), which is then inserted into the opening marked Air and allowed to remain as an air inlet to the glass air tube. The transfusion tubing is connected by introducing the end of the filtering drip chamber into the previously punctured hole marked Outlet in the stopper (Fig. 101—plasma transfusion is shown in the

illustration). The tubing is filled with blood and the transfusion is administered according to the usual technique. Use of a filtering device, either the one supplied by the manufacturer or an equally satisfactory one, is necessary when transfusions of blood or plasma are given in order to remove any fibrin or clots that may be present.

Blood stored for more than eight days is considered unsafe for transfusion as whole blood but may be used as a source of

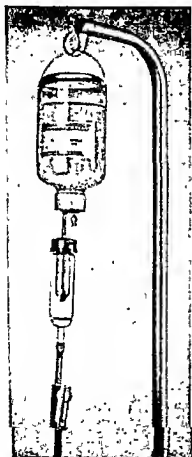


Fig. 101



Fig. 102.

Fig 101.—Transfusion is administered through a filtering drip chamber Plasma transfusion is shown. (Courtesy Cutter Laboratories, Berkeley, Calif.)

Fig 102.—Collection of plasma from stored blood, using vacuum pooling flask. (Courtesy Cutter Laboratories, Berkeley, Calif.)

plasma for transfusion. Plasma can be separated from the cells either by aspiration following sedimentation by gravity during prolonged storage or by centrifugation. When the centrifuging technique is employed, two similar flasks of blood are placed in centrifuge cups, balanced exactly by addition of the proper amount of water to the lighter cup and placed opposite each other in the centrifuge. If other flasks are to be centrifuged at the same time, each pair is balanced and placed in the centrifuge before the next pair is prepared. Centrifugation is continued for thirty minutes at a speed of 1,500 to 2,000 r.p.m., ten minutes being allowed to bring the speed to this point, and subsequent deceleration being done without braking.

For collection of plasma a vacuum pooling flask is preferable. The valve (Saftivalve) is attached to the large flask in the manner described, with the wheel closed, and the donor needle is replaced by a long aspirating needle. The top of the flask of blood is cleaned with antiseptic and the vacuum is released by insertion of a sterile needle through the hole marked Diaphragm. The hole marked Air must not be used because it is connected with the air tube; inrush of air would disturb the separated cell and plasma layers by bubbling up from the bottom. The aspirating needle is inserted through the hole marked Outlet until the point is carried below the surface of the plasma (Fig. 102) and the valve is opened slowly. Aspiration is performed most conveniently if the opening of the needle is kept turned to the side, just above the top of the cell layer. After all but a thin layer of plasma has been removed, the valve is closed before the needle opening is raised above the surface of the remaining plasma, and the aspirating needle is withdrawn from the flask. Further collections of plasma may be performed with the same apparatus by the same technique. When the pooling flask is full, the valve is withdrawn, the top of the stopper is cleaned with an antiseptic, and the protective metal cap is replaced.

Aerobic and anaerobic cultures are made from the pooled plasma. Specimens are withdrawn through the hole marked Diaphragm. If cultures are sterile after ten days, a small amount of bacteriostatic preservative is added to the plasma. A special flask (Sediflask) is supplied for storage and transfusion of blood, if plasma is to be withdrawn from over-aged units by the sedimentation technique rather than by centrifugation.

For administration, plasma is withdrawn from the pooling and storage flask into an empty sterile vacuum flask by the same technique described (Fig. 102). Plasma transfusions are administered in the same way as blood transfusions (Fig. 101).

**Intravenous Infusion Equipment (Upjohn).**—Solutions for intravenous use are prepared, sterilized, and supplied by the manufacturer in sealed flasks. The distinguishing feature of this method is the dispensing cap (Fig. 103), which consists of two

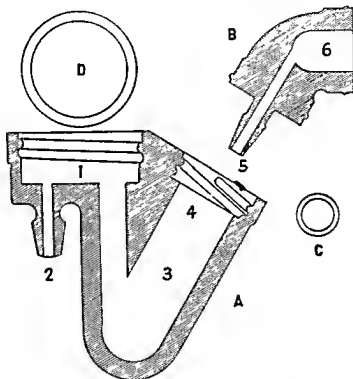


Fig. 103.—Dispensing cap for infusion equipment.  
(Courtesy The Upjohn Company, Kalamazoo, Mich.)

parts: the body, *A*, and the adapter, *B*. The cap is taken apart and cleaned thoroughly after use and is reassembled before sterilization. In assembly of the cap, the small gasket, *C*, is placed in the small opening, *4*, and clean absorbent cotton is tucked into the open end, *6*, of the adapter. The nipple end, *5*, of the adapter is inserted into the small opening, *4*, of the cap body, in which it is fixed by a quarter turn. The large gasket, *D*, is

fitted into the bottom of the large opening, 1, of the cap body and the intravenous tubing assembly is attached to the nipple, 2, of the cap body. The entire unit is placed in a pack and sterilized before use.

Prepared containers of fluid are marked both on the label and on the cap. To prepare a bottle of fluid for use, the metal cap is removed by pulling the tab downward and lifting off the cap and liners. The pack containing the sterile infusion assembly is opened and the dispensing cap is screwed over the top of the bottle (Fig. 104). If the gasket is loose, it should be replaced in the chamber with sterile forceps before the cap is attached.

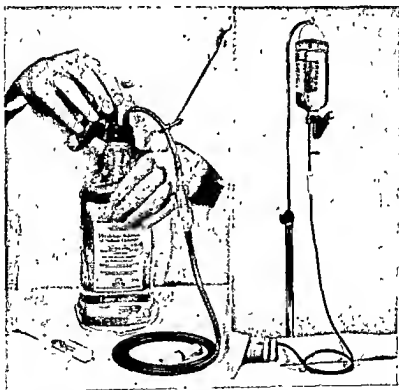


Fig 104

Fig 105.

Fig 104 — Preparation of sterile infusion assembly. (Courtesy The Upjohn Company, Kalamazoo, Mich)

Fig 105 — Infusion, rate of flow is adjusted by a screw clamp and drip chamber. (Courtesy The Upjohn Company, Kalamazoo, Mich)



The tubing is filled with fluid in the usual manner, venipuncture is performed, and the infusion is administered (Fig. 105).

**Collection and Administration of Blood Transfusions (Upjohn).**—An equipment pack for collection of blood is assembled and sterilized before use; it can be used repeatedly. The cap assembly (Fig. 106) is composed of the same parts used for administration of infusions, with the exception that the large gasket is replaced by a filter, *E*. The filter is made up of a rubber gasket holding a nickel filtering screen and an air inlet tube and may be used repeatedly. The filter is inserted into the chamber, *I*,

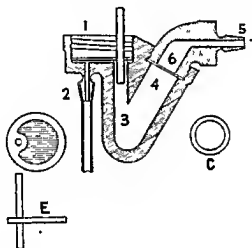


Fig. 106.—Cap assembly for collection and administration of blood transfusion (Courtesy The Upjohn Company, Kalamazoo, Mich.)

of the cap body with the short end of the filter tube entering the air inlet opening, 3, of the cap body; the long end of the filter tube projects upward. One end of a portion of rubber tubing about eighteen inches long is attached to the nipple, 5, on the adapter and a glass needle adapter is attached to the other end of the tubing. The small gasket, *C*, is placed in the chamber, 4, and the open end, 6, of the adapter is attached to the chamber, 4. A piece of rubber tubing about six inches long is attached to the nipple, 2, of the cap body. A properly cleaned 600 c.c. bottle and the appropriate needles are placed in a pack together with the cap assembly and the equipment is sterilized.

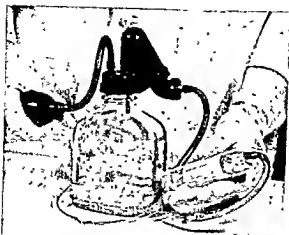


Fig 108

Fig. 107 —Anticoagulant solution is aspirated into flask by pump suction before collecting blood (Courtesy The Upjohn Company, Kalamazoo, Mich.)

Fig 108 —Collection of blood, using pump suction. For storage as a sealed sterile unit, the needle is detached, the bulb and short tubing are removed, and the end of the long tubing is slipped over the open nipple of the cap (Courtesy The Upjohn Company, Kalamazoo, Mich.)

For use the pack is opened, the cap is placed on the bottle, the adapter is tightened, and a suction bulb is attached to the short piece of tubing. Sterile sodium citrate solution (2.5 per cent) is required in the proportion of 50 c.c. for each 450 c.c. of blood. Before collection of the blood, 40 c.c. of the citrate solution is aspirated into the flask, which then is shaken sufficiently to coat the inner surfaces with citrate solution (Fig. 107). Venipuncture is performed upon the donor and blood is aspirated by gentle compression of the suction bulb (Fig. 108). After the

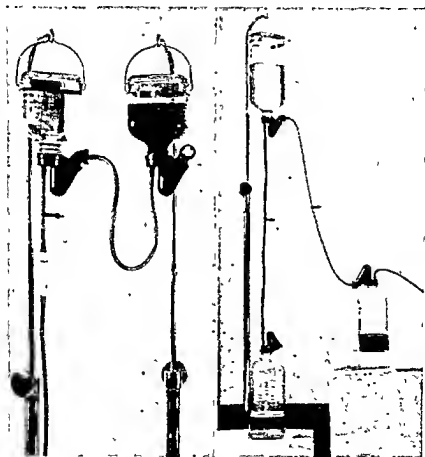


Fig. 109.

Fig. 110.

Fig. 109 --Transfusion of blood through an infusion assembly. (Courtesy The Upjohn Company, Kalamazoo, Mich.)

Fig. 110 --Wangensteen type of constant suction apparatus, using large bottles. (Courtesy The Upjohn Company, Kalamazoo, Mich.)

proper amount of blood is collected, the needle is removed from the vein and 10 c.c. of sodium citrate solution is again aspirated to prevent coagulation of blood in the tubing. The glass adapter and needle are removed from the tubing, and suction bulb and tubing are detached from the nipple of the dispensing cap. The end of the tubing previously attached to the venipuncture needle is connected to the nipple of the dispensing cap, sealing the entire unit. The bottle of blood is stored in this manner if it is not to be used at once.

For administration of the transfusion, an infusion of normal salt solution is begun. The air inlet of the infusion is removed and the corresponding cap adapter of the transfusion unit is unscrewed and attached to the open chamber of the infusion assembly (Fig. 109). The filter from the infusion bottle is attached to the open chamber of the transfusion assembly. Physiologic salt solution is the proper solution for use in this instance; Ringer's solution is not acceptable because of its calcium content and the consequent danger of coagulation. Once started, the blood transfusion will flow steadily without entering the infusion bottle. The infusion permits accurate placing of the needle without loss of blood or contamination of the set and also permits washing of all remaining blood out of the tubing.

Bottles and cap assemblies of this type can be used to make a suction drainage apparatus of the Wangenstein type (Fig. 110). Large bottles (2,000 c.c.) are used. After the assembly has been put together, both clamps on the rubber tubing are closed and the bottle containing water is hung from the standard. Suction is begun when the clamp between the gravity bottles is opened. When all the water has drained from the upper bottle to the lower, both screw clamps are closed tightly, the cap assemblies on the two bottles are interchanged, and the full bottle is hung from the standard.

# INDEX\*

## A

- Abbott-Rawson tube, 613  
 Abortion, infected, gas gangrene following, 503  
     tetanus following, 507  
     spontaneous, following operation, 226  
 Abdominal distention (*see* Distention, intestinal)  
 Abdominoperineal resection (*see* Rectum, abdominoperineal resection of)  
 Abscess, appendical, 442, 649 (*see also* Appendicitis with abscess)  
     association of bacteremia with, 353  
     of septicemia with, 353  
     following hypodermoclysis, 38  
     ischio-rectal, 689  
     liver, 652  
     lung (*see* Lung, abscess of)  
     metastatic, 353  
     pelvic, 443, 662  
     diagnosis of, 651  
     in appendical peritonitis, 651  
     treatment of, 652  
     perianal, 689  
     residual, in appendical peritonitis, 651  
     subphrenic, 443 (*see also* Subphrenic space, infection of)  
     wound, 496  
 Acacia gum in treatment of shock, 152, 156  
 Accidents to unconscious patient, prevention of, 112  
 Acetic acid in treatment of burn infection, 544  
     of wound infection, 487  
 Acetylthetamethylcholine (*see* Mecholyl)  
 Acetylsulfadiazine, 290, 339  
 Acetylsulfamerazine, 293  
 Acetylsulfanilamide, 282  
 Acetylsulfathiazole, 287, 289  
 Achlorhydria, 604  
     anemia associated with, 214  
 Acid, aminoacetic, 25  
     beta hydroxybutyric, 25  
     carbonic, 25, 28  
     hydrochloric, in gastric juice, 603  
     lactic, 25, 52  
     metabolic, 25, 26, 28, 123, 126  
     phosphoric, 25  
     sulfuric, 25

- Acid-base balance, 23, 26  
     effect of vomiting on, 25  
     in diabetes, 25  
     regulation by kidneys, 26  
     by lungs, 23  
     role of plasma proteins in, 63  
 Acidosis, 25, 123, 125  
     carbon-dioxide combining power of blood in, 28, 126  
     caused by starvation, 28, 58, 125, 320  
     by sulfanilamide, 285  
     correction of, 33, 126  
     by dextrose, 33, 126  
     by sodium chloride, 33  
     lactate, 33  
     diabetic, 268  
     simulating appendicitis, 268, 647  
     fluid replacement therapy in, 26, 33  
     in children, 190  
     postoperative, 123, 126  
     respiratory rate in, 25  
     urinary ketones in, 29, 123, 126  
 Acriflavine, 338, 356  
 Actinomyces bovis, effect of penicillin on, 297  
 Adhesions, peritoneal, 416, 641, 648, 652  
 Adhesive dressing of wound, 467  
     fixation of incision, 464  
 Adrenal cortex, changes in, in burns, 523  
     cortical extract in treatment of burns, 537  
     of shock, 154, 156  
 Adrenalin (*see* Epinephrine)  
 Adynamic ileus (*see* Obstruction intestinal)  
 Aerobacter aerogenes, effect of streptomycin on, 313  
     of sulfadiazine on, 290  
     in urinary tract infection, 340  
     resistance to penicillin, 299  
 Aerosol penicillin, 585, 590  
 Age, old, as contraindication to Avertin, 97  
     to sodium pentothal, 101  
     complicating disease in, 198  
     early ambulation in, 200  
     physical examination in, 197  
     postoperative care in, 199  
     preoperative care in, 197, 198

\*Numbers in italics indicate a fuller discussion of the subject.

- Age, old—*Cont'd*  
 psychologic factors in, 201  
 sedation in, 200  
 relation to fluid balance, 21  
   to gynecologic surgery, 781,  
   783  
   to peptic ulcer hemorrhage,  
   627  
   to pulmonary embolism, 401  
   to venous thrombosis, 383  
   to wound healing, 457, 499,  
   500
- Agranulocytosis caused by amido-  
 pyrine, 87  
   by propylthiouracil, 736  
   by sulfonamide drugs, 279, 286  
   by thiouracil, 733  
   symptoms of, 733  
   treatment of, 219, 280, 733
- Aims of postoperative care, 18  
 of preoperative care, 17
- Air in peritoneal cavity, postopera-  
 tive, 115  
   mattress, 201, 344  
   replacement in hemothorax, 568
- Alanine, 59
- Albumin-globulin ratio, 62, 65
- Albumin, serum, 62, 151, 800  
   concentrated, in treatment of  
   shock, 151  
   osmotic effect of, 62, 151  
   relation to acid base balance, 63  
   to tissue protein loss, 65  
   synthesis of, in liver, 62, 694
- Albuminuria, 256  
   in burns, 523  
   in glomerulonephritis, 254  
   in transfusion reaction, 182  
   orthostatic, 256  
   postoperative, 254
- Alcohol as anti-epileptic, 461, 466, 477  
   in skin irritation, 344  
   injection of, in pruritus ani, 683  
   oral, in occlusive arterial disease,  
   765  
   in elderly patient, 201
- Alcoholism, prophylaxis of shock  
 in, 143
- Alginate as hemostatic agents, 491
- Alkali, extracellular, 23, 24  
   intracellular, 23, 24  
   reserve, 25  
   in alkalosis, 28  
   in ketosis, 58
- Alkalis, use of, in crush syndrome,  
 141  
   in transfusion reaction, 183,  
   184  
   with sulfonamide drugs, 280,  
   286, 288, 290, 339
- Alkalosis, 25, 141  
   as caused by vomiting, 28, 190  
   carbon-dioxide combining power  
   of blood in, 28  
   correction of, 26, 34  
   excretion of bicarbonate in, 29  
   respiratory rate in, 25  
   sodium lactate contraindicated  
   in, 34
- Allantoin in treatment of sloughing  
 wound, 345, 488
- Allergic reactions to blood trans-  
 fusion, 185
- Allergy predisposing to postopera-  
 tive pulmonary atel-  
 ectasis, 364
- Alpha-tocopherol in peripheral vas-  
 cular disease, 767
- Aluminum gel in acute peptic ulcer,  
 605  
   paste as protective skin dressing,  
   659  
   powder as protective skin dress-  
   ing, 621, 659
- Alurate, 85
- Ambulation, early, 129  
   after appendectomy, 647  
   after gastric surgery, 610  
   after gynecologic surgery, 786  
   postoperative, delayed, 128
- American Red Cross, blood collec-  
 tion by, 186
- Amidopyrine, 87
- Amino acids, 59  
   as source of carbohydrate, 61,  
   693  
   deamination of, 61, 693  
   essential, 59, 61, 68, 69  
   deficiency of, 60  
   for oral administration, 72  
   for parenteral administration,  
   69, 76  
   in treatment of ulcers, 67  
   of wounds, 489  
   nonessential, 59, 61  
   oxidation of, 61  
   synthesis of, 59, 61, 693
- Aminoacetic acid, 59, 699
- Aminophylline in asthma, 319  
   in biliary colic, 708  
   in congestive heart failure, 241  
   in pyrexia with dyspnea, 242
- Ammonia, endogenous synthesis of,  
 26  
   spirits of, 234
- Ammonium chloride as diuretic, 241  
   as expectorant, 319  
   as urinary acidifier, 341  
   mandelate, 340
- Amniotic fluid concentrate, use of,  
 to prevent adhesions,  
 416

Amphetamine sulfate in hiccup, 342

Amputation, 708 (*see also* Extremity, amputation of)

Amylnitrite in angina pectoris, 248

Amylase in carbohydrate digestion, 51

  scrum, 798

  in biliary colic, 707

Amytal, 85

Anaerobic organisms in oral sepsis, 202

  in wound infection, 486, 507

Analeptic drugs in barbiturate overdosage, 86, 87

  in morphine overdosage, 90

Analgesic drugs, 87

Anastomosis, intestinal (*see* Intestine, anastomosis of)

Anchorage of drains, 494, 558

Anemia, 213, 214

  after gastric resection, 617, 626

  after hemorrhage, 213

  after hemorrhoidectomy, 683

  albuminuria in, 256

  as cause of delayed convalescence, 160

  of tachycardia, 249

  as caused by duodenal fistula, 623

  by enterostomy, 645

  as contraindication to operation, 143, 215

  associated with protein deficiency, 67

  chronic secondary, 214

  classification of, 213

  effect of, on wound healing, 457, 498, 500

  hemolytic, as caused by sulfonamide drugs, 279, 286, 287, 291

  hypochromic microcytic, 214

  in aged patient, 198

  in burns, 522, 525, 535, 546

  in carcinoma of colon, 662

  in gas gangrene, 505

  in gastric disease, 601

  in gynecologic patients, 215, 779, 781

  in hemolytic jaundice, 216

  in hyperthyroidism, 731

  in infants, 193

  in malignant disease, 214

  in malnutrition, 28

  in nephritis, 255

  in parasitic infection, 214

  in sepsis, 214, 216

  in ulcerative colitis, 657

  masked by dehydration, 78, 143

  pernicious, 217

  postoperative, use of oxygen in, 804

Anemia—Cont'd

  preoperative diagnosis of, 104, 105, 143, 215

  relation to venous thrombosis, 383

  to wound healing, 130, 457, 498, 500

  sickle-cell, 217, 249

  treatment of, 143, 162, 215

Anesthesia, basal, 96

  choice of, 97

  contraindications to, 107

  course of, 97, 112

  effect on liver, 721

  on urinary bladder, 328

  examination preceding, 104

  for drainage of infections, 756

  for pelvic examination, 780

  in angina pectoris, 248

  in cardiac disease, 230, 232, 238

  in diabetes, 270

  in hypertension, 251

  in treatment of burns, 527, 541

  intratracheal, for thyroidectomy, 748, 750

  intravenous, premedication in, 96

  local, premedication in, 95

  premedication in, 92

  protein loss following, 64

  pulmonary complications after, 108

  record of, 111

  recovery from, 112

  relation to acute gastric dilatation, 452

  to postoperative atelectasis, 365

  resistance to induction of, 97

  shock after, 139

  spinal, 99

  contraindicated in angina pectoris, 248

  in hypertension, 248, 252

  in syphilitic heart disease, 246

Anesthetic, oil-soluble, for post-hemorrhoidectomy pain, 683

Aneurysm, arterial, of extremity, 776

Angina pectoris, 248, 349

Anorectal fistula, 687

Anovemia in shock, 133, 804

Anoxia, damage to pulmonary alveoli by, 567

  in shock, 132, 136, 137, 143, 804

  relation of, to wound healing, 457

Antibiotic drugs, 275, 276

Antibodies, transport of, 63

Anticoagulant (*see* Dicumarol, Heparin)

Antihistamine drugs in penicillin reaction, 301

  in pruritus ani, 688

- Antilipotropic substances, 57  
 Antiprothrombin in blood-clotting mechanism, 163  
 Antiseptic agents, 476  
 Antiseptics contraindicated in gangrene, 768  
   in treatment of open wounds, 474  
 Antitoxin in treatment of gas gangrene, 505, 506  
   of septicemia, 356  
   of tetanus, 509  
 Anucaine, 684  
 Anuria caused by sulfonamide drugs, 280, 291  
   in liver failure, 721  
   in shock, 140  
   in transfusion reaction, 182  
   post-traumatic, 140 (*see also* Crush syndrome)  
   treatment of, 184, 261, 281  
 Anus, examination of, 680  
   fissure of, 686  
   fistula of, 687  
   plastic operation on, 689  
   pruritus of, 688  
   surgery of, preoperative preparation for, 681  
 Anxiety, 92, 103, 108  
 Apathy in dehydration, 27  
   in shock, 142  
 Aphonia after thyroidectomy, 749  
 Apparatus (*see also* special headings):  
   for blood transfusion, 174, 176, 177, 812  
   for hypodermoclysis, 36  
   for infusion, 38, 41, 812  
   intramedullary, 44  
   for leg exercise, 385  
   for proctoclysis, 36  
   for suction drainage of chest, 555, 557  
     of small intestine, 430  
     of stomach, 324, 834  
   hand-roller, for rapid transfusion, 179  
 Appendectomy in acute appendicitis, 647  
   in perforative appendicitis, 648  
     with abscess, 649  
     with generalized peritonitis, 652  
   interval, 646  
   intestinal obstruction after, 445, 652  
   with drainage, 649, 650, 653  
   without drainage, 648  
 Appendicitis, acute, 647  
   drainage in, 648, 649  
   preoperative urinalysis in, 647  
 Appendicitis—Cont'd  
   as cause of fistula, 511, 651, 653  
   of peritonitis, 442, 648  
   of subphrenic space infection, 406, 445, 649  
   delayed operation for, 649, 650  
   emergency operation for, 647, 649, 651  
   occurrence of, 646  
   perforative, 648  
     gas bacillus infection following, 503  
     local use of sulfonamides in, 285, 647  
     postoperative drainage in, 493, 649  
     surgical treatment of, 447, 648  
     use of penicillin in, 448  
   with abscess, 649  
   complications of, 650, 651  
   drainage of, 650  
   with generalized peritonitis, 652  
   wound infection after, 648  
 Appetite, loss of, in anemia, 214  
   in burns, 545  
   in carcinoma of stomach, 602, 603  
   in vitamin deficiency states, 209  
 Arginine, 59  
 Arising, postoperative, 127  
 Arrhythmias, cardiac, 232, 235, 740  
 Arterial disease, chronic occlusive, 758  
   hypertension (*see* Hypertension)  
 Arteriography, 761, 775  
 Arteriosclerosis, 758, 761, 762  
   as cause of gangrene, 758  
   diabetic, 759  
   low cholesterol diet in, 765  
   relation to wound healing, 457, 499  
 Arteriosclerotic gangrene, sympathetic ganglionectomy in, 767  
 Arteriovenous fistula, 773  
   arteriography in, 775  
   care in operating room, 776  
   diagnosis of, 774  
   operation for, 775, 777  
   physiologic effects of, 774  
   postoperative care in, 777  
   preoperative care in, 774  
 Artery, cystic, postoperative bleeding from, 717  
   intercostal, bleeding from, 564  
   thyroid, postoperative bleeding from, 750  
 Arthritis, suppurative, treatment with penicillin, 301  
 Ascorbic acid (*see* Vitamin C)  
 Aspartic acid, 59



Aspiration, diagnostic, in pulmonary disease, 376, 574, 587  
 of gastrostomy catheter, 638  
 of pharynx, postoperative, 113, 366, 590  
 in empyema, 553  
 pneumonia, postoperative, 374  
 tracheobronchial, 369, 563, 565, 566, 576, 578

Aspirin, 86, 87, 90

Asthma as caused by wet lung, 566  
 following blood transfusion, 185  
 in cardiac disease, 241  
 relation to pulmonary atelectasis, 364

Asthmatic bronchitis, 319

A. T. 10 in hypoparathyroidism, 753

Atelectasis, pulmonary, 359  
 after biliary tract surgery, 717  
 after gastric surgery, 610, 615, 618  
 after pulmonary resection, 582, 586  
 after thyroidectomy, 751  
 as caused by wet lung, 566  
 diagnosis of, 360  
 in appendical peritonitis, 651  
 in chest wound, 564  
 in hemothorax, 569  
 pathogenesis of, 359, 361  
 postoperative, 632  
 prophylaxis of, 364, 563, 577  
   breathing exercises in, 366  
   carbon dioxide inhalation in, 366, 368  
   early ambulation in, 367  
   position change in, 367  
 relation of anesthetic agent to, 365  
   of operative incision to, 365  
   of position to, 365  
   of preoperative sedation to, 364  
 treatment of, 367  
   bronchoscopy in, 371  
   carbon dioxide in, 366, 368  
   tracheobronchial suction in, 369

Atony following vagus nerve resection, 634, 636  
 gastric, 452, 610, 618

Atropine as aid in passage of Miller-Abbott tube, 431

use of, in biliary colic, 708  
   drainage, 714, 715  
   in morphine overdosage, 90  
   in nausea, 120  
   in paroxysmal dyspnea, 242  
   in peptic ulcer, 606

Atropine, use of—Cont'd  
   in postoperative bronchoscopy, 565, 576  
   in preoperative medication, 93  
   in pulmonary embolism, 405  
   in syncope, 233  
   in tetanus, 511  
   with Mecholyl, 235

Auricular fibrillation, 236, 243  
 in thyrocardiac disease, 740  
 flutter, 235

Auscultation in diagnosis of intestinal obstruction, 419, 423, 424, 440

in diffuse peritonitis, 449

Autolysis of liver cells, postoperative, 721

Avertin as basal anesthetic, 96  
 contraindications to use of, 97  
 indications for, 96, 97, 232, 251, 511  
 method of administration, 96  
 relation to pulmonary atelectasis, 364

Avitaminosis (see Vitamin deficiency)

Azochloramid in wound infection, 485, 674, 677, 689

## B

*Bacillus brevis*, 483  
*pyocyaneus* (see *Pseudomonas aeruginosa*)

Bacitracin, 484

Backache, postoperative, 111, 115

Bacteremia, 313

Bacteria, effect of bacitracin on, 484

\* penicillin on, 297, 303, 481  
 streptomycin on, 310, 482  
 sulfadiazine on, 290  
 sulfanilamide on, 282  
 sulfathiazole on, 287  
 sulfonamide drugs on, 277, 479  
   for intestinal antiseptics, 293  
   for urinary antiseptics, 296  
 tyrothricin on, 483  
 zinc peroxide on, 486

Bactericidal agents, 474

Bacteriology of burns, 543

of empyema, 550  
 of gas bacillus infection, 503  
 of peritonitis, 444  
 of skin flora, 477  
 of wound infection, 496

Bag, colostomy, 678

ileostomy, 659

Balsam of Peru, 488

Bandage, elastic, postoperative use of, 386

- Barbitol, 85 (*see also* Sedation)
- Barbiturate drugs, 84 (*see also* Sedation)
- excretion of, 86
  - in kidney damage, 86
  - in liver damage, 86
  - in preoperative medication, 93
  - intermediate acting, 85
  - long-acting, 85
  - overdosage with, 86
  - short-acting, 85
  - toxic reactions to, 86
- Barium enema in carcinoma of colon, 661, 662, 664
- preparation for, 804
  - meal contraindicated in carcinoma of colon, 662
  - in intestinal obstruction, 421, 642
  - use of, with Miller-Abbott tube, 434, 435
- Basal metabolic rate, increased, 724, 726
- reduction of, 726, 732, 737, 738
- Bed, anesthetic, 112
- oscillating, 766
  - rest in cardiac disease, 240
  - postoperative, 127
  - preoperative, in thoracic surgery, 571
  - relation to venous thrombosis, 240 381
- Benacrol, 684
- Benadryl, 185, 301, 688
- Benedict's test for urinary sugar, 272
- Benzedrine in hiccough, 342
- Benzoïn, tincture of, as protective skin dressing, 621, 659
- Beta-hydroxybutyric acid, 25
- Bicarbonate ion, 24
- plasma, 25
- Bicarbonate-carbonic acid ratio of plasma, 25
- Bile, administration of, postoperative, 713
- composition of, 694
  - deficiency of, in bleeding tendency of jaundice, 219, 705
  - drainage of, 711, 713
  - duct, common, drainage, 711
  - ducts, injury to, 718
  - examination of, before removal of T-tube, 715
  - excretion of, 694
  - flow, Carter's food test of, 713
  - functions of, 694
  - in stool, 694, 695, 704
  - in urine, 695, 704
  - pigments, in bile, 694
- Bile—Cont'd
- salts, as chologogue, 715
  - excretion of, 694
  - in absorption of vitamin K, 212, 213, 705, 706
  - in bile, 694
  - in digestion of fats, 54, 56
- Biliary colic, treatment of, 707, 714
- fistula, 56, 716
  - peritonitis, 720
  - tract, disease of, with cardiovascular disease, 692
  - effect on liver, 692
  - examination of blood in, 702
  - drainage tube, removal of, 715
  - incisional drainage, postoperative, 492
  - obstruction of, jaundice in, 695, 704
  - stones in, postoperative, 714, 719
  - surgery of, blood loss in, 160, 710
  - postoperative care in, 709
  - complications in, 717
  - hemorrhage in, 717
  - preoperative care in, 692
- Bilirubin, excretion of, 694
- formation of, 693
  - in bile, 694
  - serum, 798
  - in jaundice, 697, 704
- Binder for wound dressing, 469, 595
- Biopsy, diagnostic, 572, 661
- Bi-muth subcarbonate in colostomy diarrhea, 679
- Bladder, urinary (*see* Urinary bladder)
- Bleeding tendency (*see* Hemorrhagic tendency)
- Blood bank, autolysis in, 186
- prothrombin in, 187
  - reactions to, 187
- banks, 185
- calcium of, 798
  - in hypoparathyroidism, 752
- carbon-dioxide combining power of, 25, 28, 33, 126, 798
- carbonic acid of, 25
- chemistry in burns, 522, 523
- in dehydration, 27
  - in diabetes, 263, 266, 268
  - in hiccough, 343
  - in intestinal obstruction, 417, 425
  - in peritonitis, 449
  - in pyloric obstruction, 609
  - in uremia, 260
  - normal values, 798
- chloride (*see* Chloride)

**Blood—Cont'd**

- clotting mechanism of, 163
  - in hemophilia, 218, 226
  - in hypoprothrombinemia, 219, 226, 702
  - in purpura, 224, 226
  - in scurvy, 218, 226
- coagulability of, in venous thrombosis, 381, 382
- cold agglutinins in, 168
- collection of, for transfusion, 175, 815, 824, 831
- count, normal, 163
- cross-matching of, 165, 167, 168
- culture, in septicemia, 354
- determination of group, 166
- dilution following hemorrhage, 148, 351
- examination of, in biliary tract disease, 702
  - in dehydration, 27
  - in kidney disease, 258
  - preoperative, 104, 105
- hydrogen-ion concentration of, 25
- increased coagulability of, postoperative, 382
- iodine, 737, 799
- loss during operation, 19, 159
  - from hemorrhoids, 214
  - in burns, 522, 542
  - in intestinal obstruction, 421
  - in menorrhagia, 215
  - in postoperative hemorrhage, 495
  - in ulcerative colitis, 658
- nonprotein nitrogen of (*see* Non-protein nitrogen)
- osmotic pressure of, 62
- pH of, 25
- phosphorus of, in hypoparathyroidism, 752
- plasma (*see* Plasma)
- postoperative changes in, 382
- preservation of, 185
- pressure as factor in postoperative hemorrhage, 717
  - effect of Pitressin on, 327
    - of stimulant drugs on, 144, 145
    - of transfusion on, 352
- in peptic ulcer hemorrhage, 627, 628
- in postoperative hemorrhage, 350
- in pulmonary embolism, 402
- in shock, 132, 135, 137, 142, 350
- in spinal anesthesia, 100
- preoperative determination of, 104

**Blood pressure—Cont'd**

- restoration of, in shock, 146
- stabilization of, by plasma proteins, 62
- Rh type, 169
  - blocking antibodies, 173
  - determination of, 171
  - sensitization, 170, 173
- serologic groups, 165
  - determination of, 166
- serum (*see* Serum)
- sickling test, 217
- sugar (*see* Sugar)
- transfusion (*see* Transfusion)
- typing, 166
- viscosity of, 62, 804
- volume in burns, 525, 535, 536
  - in chronic protein deficiency, 69
  - in dehydration, 65, 66
  - in hemolytic jaundice, 705
  - in shock, 139, 142, 149
  - in uremia, 260
  - preoperative restoration of, 106
  - variations in, 66
- Body heat, conservation of, in children, 195
  - maintenance of, after operation, 112, 117
  - regulation of, 22, 117
- surface, evaporation from, 22, 122, 123
- weight, blood plasma content of, 21
  - water content of, 21
- Boils, postoperative, 346
- Bone marrow concentrate in agranulocytosis, 280, 734
- Borborygmi, 419, 423
- Boric acid as antiseptic, 466, 475
  - as bladder instillation, 333
  - as dressing in burns, 526
  - as eye irrigation, 317
  - as wet dressing, 471
- Bovine serum albumin, 153
- Branham's sign, 774
- Breathing exercises, postoperative, 367, 385, 560
- Bromides, contraindications to use of, 83
  - in hyperthyroidism, 730
  - intoxication caused by, 83
- Bromsulfalein test of liver function, 697, 702
- Bronchial fistula following pulmonary resection, 580, 582
  - in empyema, 561
  - in lung abscess, 587, 589
  - in traumatic chest wounds, 564, 567

**Bronchial**—Cont'd  
 obstruction as cause of pulmonary atelectasis, 359, 361

**Bronchiectasis, bronchography in**, 573, 584  
 detection of, 198, 584  
 following empyema, 551  
 in aged patient, 198  
 preoperative postural drainage in, 575, 584  
 pulmonary resection for, 583

**Bronchitis, postoperative**, 318, 349, 358  
 preoperative, 107

**Bronchiography, diagnostic, in thoracic surgery**, 573, 584

**Bronchopneumonia, postoperative**, 319, 359, 365, 372

**Bronchoscopy, 371**  
 diagnostic, preoperative, 572, 584, 596  
 during operation, 365, 590  
 in lung abscess, 586  
 in wet lung, 566  
 postoperative, 366, 562, 576, 578, 582, 590

**Buerger's disease (see Thromboangiitis obliterans)**

**Buffer system, carbon dioxide**, 25

**Burns, 519**  
 anemia in, 522, 525, 535, 546  
 blood changes in, 522, 523  
 transfusion in, 68, 525, 535, 545, 546  
 cleansing of, 526  
 complications of, 523, 525  
 debridement of, 526  
 diet in, 545  
 dressing of, 540, 544  
 materials for, 469  
 drugs in local treatment of, 539, 544  
 effect of, on adrenal cortex, 523  
 estimation of surface area involved, 532, 533  
 first degree, 519  
 fluid replacement in, 532, 534, 537  
 healing of, 520, 521, 540, 541  
 hemoconcentration in, 524, 527, 532, 534  
 infection of, 520, 524, 525, 534, 538, 543, 544  
 intermediate degree, 520, 525, 540  
 kidney damage in, 522, 524  
 liver damage in, 522, 524  
 local fluid loss in, 520, 524  
 mental depression in, 523, 525  
 morphine in, 532  
 of extremities, 530  
 of face, 531

**Burns**—Cont'd  
 of perineum, 531  
 oliguria in, 534  
 pain in, 520, 523, 525  
 pathology of, 519  
 plasma loss in, 522, 523, 532  
 transfusion in, 68, 525, 532, 533, 534, 536, 545  
 plaster dressing in, 530  
 pneumonia in, 524, 525  
 pressure dressing in, 526  
 protein loss in, 64, 520, 523, 524, 545  
 replacement therapy in, 68, 545  
 reduction of blood volume in, 524, 535, 536  
 respiratory tract involvement in, 537  
 scarring in, 519, 525  
 second degree, 519, 525, 540  
 shock in, 523, 525, 532, 535  
 skin grafting in, 525, 541  
 slough in, 520, 521, 525  
 stomach ulcer in, 523  
 tanning agents in, 522, 525, 526  
 tetanus, antitoxin in, 532, 538, 539  
 associated with, 507, 509  
 third degree, 520, 525, 540  
 toxemia in, 524  
 treatment of, 525, 544  
 adrenal cortical extract in, 537  
 fluid balance chart in, 537  
 penicillin in, 537, 539, 544  
 pyruvic acid in, 543  
 streptomycin in, 539, 544  
 sulfadiazine in, 539  
 urinary output in, 68, 535  
 vitamin requirements in, 546

**Dutyn for anesthetization of nasopharynx**, 430, 435

## C

**Cachectic disease, protein deficiency in**, 64  
 as contraindication to Avertin, 97

**Caffeine in shock**, 146, 155

**Calcium bilirubinate in bile**, 716  
 blood, in hypoparathyroidism, 752, 798  
 carbonate in bile, 716  
 chloride in hypoparathyroidism, 752  
 content of normal blood, 798  
 gluconate in hypoparathyroidism, 752  
 in blood-clotting mechanism, 163  
 in hyperthyroidism, 730

Calcium—Cont'd  
 lactate in hypoparathyroidism, 753  
 mandelate, 341  
 metabolism, relation of vitamin D to, 212  
 Calculi, urinary, in sulfonamide therapy, 280, 281  
 Calmitol, 688  
 Caloric requirements, 125  
   in hyperthyroidism, 730  
 Cannula for continuous infusion, 41  
 Capillary fragility, test for, 218  
   permeability in shock, 135, 137, 804  
 Carbohydrate (*see also* Dextrose):  
   absorption of, 51  
   administration of, after operation, 125, 200  
   before operation, 106, 198  
   in children, 192, 193, 195  
   in diabetes, 263  
   in coma, 268, 269  
   postoperatively, 271, 272  
   preoperatively, 265, 269  
   in jaundice, 704  
   in liver damage, 703  
   in septicemia, 356  
   in thyroid disease, 730, 731, 743  
   routes of, 38  
   daily requirement of, 78, 126  
   digestion of, 50  
   formation of fat from, 55  
   insufficient intake of, 28, 125  
   metabolism, 50, 51, 126  
   role of liver in, 51, 125, 693  
   of vitamin B in, 79, 209, 210  
   protein-sparing action of, 52, 78, 126  
   storage of, 51, 53  
 Carbon dioxide, administration of,  
   in hiccough, 342  
   in pulmonary atelectasis, 366, 368  
   prophylactic, 385, 578, 610, 631, 672, 710, 746, 751  
   buffer system, 25  
   combining power of blood, 25, 798  
   in acidosis, 28, 268  
   in alkalosis, 28, 33  
   in diabetes, 263, 268  
   elimination of, 23, 24, 25  
 Carbonic acid, 25  
   acid-bicarbonate ratio, 25  
 Carbuncle, 266, 346  
 Carcinoma (*see also* organ involved):  
   anemia due to, 214  
   delaying effect of, on wound healing, 457, 500

Carcinoma—Cont'd  
   of colon, 661  
   of gastrointestinal tract, bleeding, 214  
   of liver, 697, 707  
   of lung, 572, 573, 574, 575  
   of rectum, 675, 680  
   of stomach, 600, 602, 604, 607  
   of thyroid, 750  
 • Cardiac arrhythmias, major, 235  
   minor, 232  
   asthma, 241  
   damage in hypertension, 250  
   disease as contraindication to cyclopropane, 98  
   to Pitressin, 327  
   to spinal anesthesia, 99, 246, 248, 252  
   blood transfusion in, 164  
   coronary, 247, 403  
   ether anesthesia in, 99, 232, 238, 248  
   evaluation of, 230  
   fluid replacement therapy in, 34, 239  
   functional, 237  
   in diabetic patient, 262  
   in hyperthyroidism, 739 (*see also* Thyrocardiac disease)  
   in surgical patient, 229  
   relation to pulmonary embolism, 378, 401  
   to surgical mortality, 230, 236, 237, 247, 248  
   to venous thrombosis, 383  
   to wound healing, 457, 499  
   rheumatic, 236  
   syphilitic, 246  
   use of oxygen in, 239, 805  
   valvular, 237  
 enlargement as caused by arterio-venous fistula, 774  
 failure, 239  
   after thoracic surgery, 581, 594  
   after total gastrectomy, 615  
   congestive, 236  
   differentiation from pulmonary embolism, 403  
   from shock, 133  
   evidences of, 230, 238  
   in auricular fibrillation, 236  
   in hyperthyroidism, 740, 744  
   treatment of, 741  
   in pulmonary embolism, 403  
   treatment of, 239  
   digitalis in, 244  
   diuretics in, 241  
 function, investigation of, 230, 692, 728

**Cardiac—Cont'd**

- irregularities caused by cyclopropane, 98
- murmurs, 230, 249
- reserve, evaluation of, 230
- in cardiac valvular disease, 238
- in thyroid disease, 727, 739
- symptoms due to excess fluid administration, 261
- valvular disease, 237

**Cardiovascular disease associated with biliary tract disease, 692****Carotid sinus, 234, 235****Carrel-Dakin irrigation, 474, 481****Carter's test of bile flow, 713, 716****Cascin as source of protein hydrolysate, 70****in diet, 70, 489, 621****lipotropic effect of, 57****Cast, plaster, in dressing of burns, 530****Casts, urinary, 256****in crush syndrome, 140, 141****Catgut, allergy to, as cause of wound dehiscence, 500****Catharsis after hemorrhoidectomy, 682****preoperative, 109****in colon surgery, 663****Cathartics, avoided in colostomy, 679****in congestive heart failure, 241****Catheter, gastrostomy, 637****intercostal, fixation of, 555, 559****in treatment of empyema, 553, 558****intranasal, for administration of oxygen, 809****retention bladder, 335, 676****in gynecologic surgery, 787****in rectal surgery, 676****Catheterization of urinary bladder, 333****in aged patient, 201****in surgery of rectum, 676****postoperative, 333, 787****preoperative, 109, 784****of ureters in sulfonamide block, 281****preoperative, 792, 793****Cavity, obliteration of, in empyema, 552, 661****Cecostomy in obstruction of colon, 667****Cedilanid, 236, 245****Cellulitis after intramedullary administration of fluids, 48****in diabetes, 266****Cellulitis—Cont'd****treatment of, 355, 756****with septicemia, 355****Cellulose, oxidized, as hemostatic agent, 491****Cement as protective skin dressing, 659****Cephlin, 55****cholesterol flocculation test of liver function, 701, 702****Cerebral damage in hypertension, 250****Cervicitis, preoperative treatment of, 782****Cevitamic acid (see Vitamin C)****Charcoal in diagnosis of fistula, 513, 792****Chart, fluid balance, 27, 123, 324, 330****in burns, 537****in duodenal fistula, 622****in enterostomy, 645****in ileostomy, 660****in intestinal obstruction, 425****notation of drains on, 788****notations on, 11****Chemotherapeutic drugs, 275****Chest, drainage of, 553****• by intercostal catheter, 553, 555****by rib resection, 557****by thoracentesis, 553****closed, 553****following decortication, 562, 570****pulmonary resection, 580, 582, 583, 596****thoracic surgery, 562****total gastrectomy, 616****in empyema, 553, 570****in lung abscess, 588****examination of, preoperative, 104, 110, 192, 198****hemorrhage into, postoperative, 351, 563, 581, 582****pain as symptom of pulmonary embolism, 402****of subphrenic space infection, 409****of venous thrombosis, 384****sucking wound of, 548, 564****surgery of, bronchoscopy following, 562, 576, 590****care during operation, 576, 590****elective, 570****intercostal block following, 562, 565, 578****physiologic considerations in, 549**

**Chest surgery—Cont'd**  
 postoperative care in, 562, 566, 577, 590  
 drainage in, 562, 576, 590  
 preoperative studies in, 572  
 use of penicillin following, 562  
 tension pneumothorax in, 567  
 traumatic wounds of, 563, 564  
 wound of as cause of tension pneumothorax, 567  
 effects of, 548  
 foreign body in, 564  
 indications for surgery in, 564, 565  
 thoracentesis in, 564  
 thoracoabdominal, 564  
 treatment of, 565  
 x-ray of, in aged patient, 198  
 in infant, 192  
 in thyroid disease, 729

**Cheyne-Stokes respiration, 242**

**Children, blood chemistry studies in, 194**  
 transfusion in, 193, 195  
 diabetes in, 263, 269  
 dosage of drugs in, 88  
 emotional reactions of, 191  
 ether anesthesia in, 99  
 fluid replacement therapy in, 193, 195  
 requirements in, 193  
 postoperative care in, 195  
 preoperative care in, 192  
 examination of, 191  
 medication in, 93  
 permission for operation in, 103  
 x-ray of chest in, 105  
 problems in care of, 190  
 respiratory tract infection in, 192  
 sinus arrhythmia in, 233  
 surgical risk in, 190  
 use of narcotics in, 119  
 vitamin therapy in, 194

**Chill, albuminuria following, 256**  
 as symptom of pyelophlebitis, 652  
 of thrombophlebitis, 384  
 of urinary tract infection, 337  
 caused by penicillin, 300  
 following blood transfusion, 183, 184

**Chloral hydrate, 83, 240**

**Chloramine-T in treatment of infected wounds, 485**

**Chloride, blood, in diffuse peritonitis, 449**  
 ion, 24, 25, 26, 30, 31  
 in alkalosis, 25, 26, 28  
 in dehydration, 28  
 loss of, by vomiting, 25, 28, 190, 320, 417, 444

**Chloride loss—Cont'd**  
 from ileostomy, 660  
 in intestinal obstruction, 417, 418, 425  
 plasma, 798  
 restoration of, 31  
 shift, 24

**Chlorazodin in treatment of infected wounds, 485**

**Chloroform, 99**

**Chlorophyll in treatment of wounds, 347, 488**

**Cholangiography, 714, 716**

**Cholangitis, postoperative, 716**  
 preoperative, 692

**Cholecystectomy, injury of bile ducts during, 718**  
 postoperative care in, 710

**Cholecystography, 698, 803**  
 contraindications to, 708

**Cholecystostomy, postoperative care in, 711**

**Choledochostomy, postoperative care in, 711**

**Cholesterol, antilipotropic effect of, 57**  
 esters, serum, 799  
 in bile, 694, 716  
 in thyroid disease, 729  
 low, diet, 765  
 serum, 799  
 solubility of, 695

**Choline, lipotropic effect of, 56**  
 use of, in liver damage, 703

**Chvostek's sign, 752**

**Cigarette drains, 492**

**Circulatory failure, peripheral (see Shock)**

**Cirrhosis, 64, 703**

**Clark's rule for dosage of drugs, 88**

**Claudication, intermittent, 758, 767**

**Climate, relation to venous thrombosis, 383**

**Closed drainage (see Empyema)**  
 loop in intestinal obstruction, 418, 420, 440

**Clostridia as cause of gas gangrene, 503**  
 in wound infection, 486  
 normal habitat of, 503, 507

**Clostridium histolyticum, 503**  
 noryi, 503  
 septicum, 503  
 sordellii, 503  
 tetani, 507  
 in burn infections, 538  
 welchii, 503, 505  
 in diffuse peritonitis, 444

- Clotting activity, blood, heparin tolerance test of, 382  
 postoperative, 381, 382  
 mechanism, 163  
 disturbances of, 163, 218, 705  
 in hemophilia, 218, 226  
 in jaundice, 219, 226, 705  
 in purpura, 224, 226  
 in scurvy, 218, 226
- Cocaine for anesthetization of nasopharynx, 371, 430
- Codeine, 86, 90, 118  
 as cough sedative, 319
- Cod liver oil in treatment of wounds, 489
- Cold agglutinins, 168
- Colectomy for ulcerative colitis, 656, 661
- Colic, absence of, in paralytic intestinal obstruction, 440  
 biliary, postoperative, 714  
 treatment of, 707  
 in mechanical intestinal obstruction, 419, 420, 423, 424
- Colitis, ulcerative, 656  
 astringent enema in, 657  
 blood loss in, 658  
 debility in, 657  
 penicillin in, 657  
 postoperative care in, 658  
 preoperative care in, 428, 657  
 streptomycin in, 657  
 sulfasuxidine in, 656  
 sulfathalidine in, 656
- Collateral circulation, estimation of, 776
- Collodion dressing, 470
- Colon bacillus (see *Escherichia coli*)  
 carcinoma of, diagnosis of, 661  
 multiple stage operation for, 662  
 preoperative care in, 661  
 single stage operation for, 663, 668  
 symptoms of, 680  
 with obstruction, 665  
 without obstruction, 663
- clostridia in, 503
- disease of, as contraindication to Avertin, 97
- obstructed, decompression of, 666
- obstruction of, 665
- obstructive resection of, 670
- preoperative preparation of, 294, 295, 428, 661
- primary anastomosis of, 668
- reduction of bacteria in, 294, 663
- resection of, as indication for use of Miller-Abbott tube, 427, 428
- Colon—Cont'd  
 surgery of, gas gangrene following, 503  
 intestinal anti-epsis in, 293, 663, 674  
 postoperative care in, 668  
 complications in, 669  
 preoperative x-ray in, 664  
 progress in, 663  
 proximal decompression in, 664  
 wound infection after, 674
- Colostomy, closure of, 672  
 complementary, 665  
 diet, 678, 802  
 dressing of, 671  
 in obstruction of colon, 666  
 in treatment of burns of perineum, 531  
 irrigation of, 678  
 permanent, care of, 678  
 postoperative complications of, 672  
 preliminary, 665, 666, 667, 670  
 prolapse of, 679  
 proximal, in fecal fistula, 792  
 in surgery of colon, 664  
 retraction of, 672, 674
- Colpotomy, 652
- Coma in diabetes, 268  
 in liver failure, 720  
 in thyroid crisis, 743, 748
- Compatibility of blood types, 166
- Complications of continuous infusion, 43  
 of fluid replacement therapy, 34, 43  
 of intramedullary administration of fluids, 48  
 postoperative (see Postoperative complications)
- Compound fractures, gas gangrene after, 504  
 tetanus after, 507
- Congenital hypertrophic pyloric stenosis, 22, 194
- Congestive heart failure, 239 (see also Cardiac failure)
- Conjugation of sulfonamide drugs, 278, 287, 290, 292, 296
- Conjunctivitis as toxic effect of sulfathiazole, 289  
 postoperative, 317
- Constant suction (see Suction drainage)
- Continuous infusion, 40
- Convalescence, slow, role of anemia in, 160
- Coramine in morphine overdosage, 87, 90  
 in shock, 146



- Coronary disease, differentiation from pulmonary embolism, 403  
in association with hypertension, 253  
thrombosis, 247
- Coryza caused by bromide intoxication, 83  
preoperative, 107, 192
- Cough as caused by wet lung, 566  
forced, in treatment of atelectasis, 367  
in congestive heart failure, 240  
preoperative, 107  
sedation of, 90, 319
- Creatinine, serum, 258, 800
- Crisis, hemoclastic, 705  
thyroid (*see* Thyroid crisis)
- Crush syndrome, 140  
treatment of, 141, 156
- Crushing injury, albuminuria in, 256  
alkalinization of urine in, 33  
of phrenic nerve, 343
- Culture, bacterial, in postoperative wound infection, 498  
throat, in pharyngitis, 318
- Curare, use of, in tetanus, 511
- Curling's ulcer, 523
- Cyanosis, 122  
as caused by sulfanilamide, 286  
as indication for oxygen, 577, 804  
as symptom of pulmonary atelectasis, 360  
embolism, 402  
following use of Avertin, 97  
methemoglobin in, 286, 804  
postanesthetic, 113
- Cyclopropane, 98, 99, 270
- Cystic artery (*see* Artery)
- Cystine, 59
- Cystitis, postoperative, 337, 676
- Cystocele as cause of urinary retention, 676

## D

- Dakin's solution, 485, 488
- Deafness caused by streptomycin, 314
- Deamination, 61
- DeBakey transfusion apparatus, 174
- Debility as indication for transfusion, 162, 215  
as result of malnutrition, 205  
depression of liver function in, 56, 57  
edema in, 205  
in carcinoma of stomach, 600  
in chronic empyema, 551  
ketosis in, 57  
postoperative foot drop in, 116  
parotitis in, 410

- Debility—Cont'd  
protein therapy in, 76  
relation to acute gastric dilatation, 452  
to delayed wound healing, 419  
to pulmonary atelectasis, 364  
to septicemia, 353  
to venous thrombosis, 383
- Débridement of burn, 526, 527, 543  
of wound, 467, 477, 481
- Decapsulation of kidney, 261, 281
- Decompression of biliary tract, 712  
of gastrointestinal tract (*see* Suction drainage)  
of intestine by enterostomy, 439, 450, 644
- Decortication in empyema, 561  
in hemothorax, 569
- Decubitus ulcer, 115, 201, 343, 344
- Dehiscence of wound (*see* Wound, dehiscence of)
- Dehydration (*see also* Fluid balance, Fluid replacement therapy, Electrolyte balance, etc.).  
acidosis in, 28, 123, 320, 647  
correction of, 66, 78, 123  
evidences of, 27  
following diarrhea, 190  
excessive water intake, 26  
fluid loss, 21, 190, 320  
vomiting, 190, 320  
hemoconcentration in, 27, 65, 66  
in acute appendicitis, 647  
gastric dilatation, 453  
in aged patient, 198, 200  
in anemia, 28, 78, 214  
in biliary tract disease, 709, 717  
in carcinoma of colon, 662  
in child, 190  
in diabetes, 262, 270  
in gastric disease, 601, 604  
in gastrointestinal tract disease, 21, 27  
in hyperthyroidism, 730, 743  
in hypoproteinemia, 63, 65, 66, 69, 78  
in ileostomy, 660  
in intestinal obstruction, 417, 420  
in postoperative parotitis, 410  
in pulmonary atelectasis, 382, 386  
in ulcerative colitis, 657  
in uremia, 260  
ketone bodies in, 28  
nonprotein nitrogen of blood in, 29  
plasma proteins in, 65, 66  
postoperative, 123, 785  
preoperative, 106  
prophylaxis of shock in, 143

Dehydration—Cont'd  
 serum albumin transfusion in, 152  
 urinalysis in, 28  
 use of Avertin in, 97  
 Delay, danger of, in intestinal obstruction, 415, 424, 426, 436  
 Delirium in thyroid crisis, 743, 748  
 Demerol, 91, 118, 628, 708  
 Depression in burns, 523, 525  
   in sulfonamide therapy, 279, 285, 289  
 Dermatitis as caused by penicillin, 300  
   by sulfonamides, 279, 285, 289, 291  
   by thiouracil, 733, 734  
   in obese patient, 204  
 Dermatome, 542  
 Desensitization, 509  
 Desoxycorticosterone in treatment of burns, 537  
   of shock, 154  
 Detoxifying function of liver, 694  
 Dextrose solution (*see also* Fluid replacement therapy)  
   administration of, 30, 31  
   by hypodermoclysis, 38  
   in infants, 193, 194, 196  
   by infusion, 38  
   intramedullary, 47  
   by proctoclysis, 35  
   during operation, 111, 143  
   in acidosis, 33, 125  
   in acute appendicitis, 647  
   gastric dilatation, 453  
   in anuria, 184  
   in biliary tract disease, 703, 704, 709  
   in burns, 535, 538  
   in children, 193  
   in congenital hypertrophic pyloric stenosis, 194  
   in congestive heart failure, 420  
   in dehydration, 30, 31  
   in diabetes, 265, 269, 271  
   in diffuse peritonitis, 448  
   in emergency operation, 110, 647  
   in enterostomy, 645  
   in hyperthyroidism, 731, 743  
   in ileostomy, 660  
   in insulin overdosage, 636  
   in intestinal obstruction, 425  
   in jaundice, 704  
   in maintenance of fluid balance, 30, 31, 32, 33  
   in malnutrition, 106  
   in nausea, 120  
   in nephritis, 259  
   in sulfonamide toxicity, 280, 281, 287

Dextrose, administration of—Cont'd  
   in ulcerative colitis, 658  
   in uremia, 260, 261  
   in vomiting, 320  
   hypertonic, 34, 35, 200, 261  
   postoperative administration of, 32, 125, 126, 576, 579, 590, 612, 613, 709  
   preoperative administration of, 106, 601, 607, 609, 630, 631  
   use of protein hydrolysate with, 76  
 Diabetes, 261  
   acid-base balance in, 25  
   anesthesia in, 99, 270  
   as cause of fatty liver, 56, 57  
   associated with hyperthyroidism, 267  
   with occlusive arterial disease, 266, 759, 764, 768  
   carbuncles in, 346  
   control of blood sugar in, 263, 271  
   decubitus ulcer in, 344  
   hepatic changes in, 56, 57  
   glycogen in, 262, 263  
   in children, 269  
   infections in, 266  
   ketosis in, 28, 58  
   preoperative care in, 262, 263, 265  
   relation to wound healing, 457, 499, 500  
 Diabetic acidosis, 58, 268  
   differential diagnosis in, 267  
   arteriosclerosis, 759, 764, 768  
   coma, 268  
   gangrene, 267, 768  
 Diagnosis, differential, of abdominal emergency in diabetic patient, 267  
   of intestinal obstruction, mechanical 415, 419, 652  
   incomplete, 641  
   paralytic, 440  
   of jaundice, 695, 704  
   of pulmonary embolism, 401  
   of acidosis, 28, 29, 56  
   of acute appendicitis, 646, 647  
   with abscess, 650  
   gastric dilatation, 451, 619  
   of alkalosis, 28, 29  
   of anemia, 28, 214  
   of barbiturate overdosage, 86  
   of carcinoma of colon, 661  
   of rectum, 680  
   of fistula, 513  
   of gas gangrene, 504  
   of hemorrhage, postoperative, 350, 495  
   of hemorrhagic tendency, 218  
   of hypoproteinemia, 28, 63  
   of lung abscess, 375

## Diagnosis—Cont'd

- of morphine overdose, 90
- of occlusive arterial disease of extremity, 761
- of parathyroid tetany, 752
- of pelvic abscess, 651
- of peritonitis, generalized, 444
- spreading, 650
- of phlebotrombosis, 383
- of postoperative complications, 19
- of pulmonary atelectasis, 360
- edema, 35
- of pyelophlebitis, 652
- of septicemia, 334
- of shock, postoperative, 350, 495
- primary, 133
- secondary, 141, 144
- of subphrenic space infection, 409, 651
- of tetanus, 508
- of thrombophlebitis, 384
- of thyroid crisis, 743, 748
- of transfusion reaction, 179, 182, 184
- of urinary tract infection, 337
- of vitamin deficiencies, 207
- of wound dehiscence, 500
- infection, 497
- preoperative in thoracic surgery, 572

## Dial, 85

Diaphragm, irritation of, as cause of hiccup, 342

## Diarrhea, effects of, 190

- following vagus resection, 634
- in hyperthyroidism, 727, 743, 748
- in permanent colostomy, 679
- in ulcerative colitis, 657, 658
- infantile, loss of potassium in, 33
- vitamin K deficiency in, 212

## Diathermy in anuria, 261, 281

in peripheral vascular disease, 117

## Dicumarol as cause of postoperative hemorrhage, 790

- contraindications to use of, 390
- in arterial surgery, 777
- in occlusive arterial disease, 767
- in prophylaxis of venous thrombosis, 387

in treatment of venous thrombosis, 390

- method of administration of, 390
- overdosage, treatment of, 392
- use of, with heparin, 391

## Diet after gastrectomy, 612, 616, 625

- after hemorrhoidectomy, 683
- as cause of fatty liver, 56
- colostomy, 678, 802
- corrective therapy, 78

## Diet—Cont'd

- gastrostomy, 638
- high fat, effect of, on liver, 57
- protein, 70
- for tube feeding, 74, 75
- in anemia, 216
- in burns, 545
- in ileocolitis ulcer, 345
- in disease, 79
- in empyema, 560
- in liver damage, 57, 703
- in wound infection, 476
- preoperative, 106, 107
- supplementary feedings in, 71, 72
- in acute inflammatory peptic ulcer, 605
- in aged patient, 198, 200
- in anal incontinence, 687
- in anemia, 216
- in bleeding peptic ulcer, 629, 630
- in children, preoperative, 192
- in colon surgery, 662, 669
- in congestive heart failure, 240
- in diabetes, 263, 272
- in dumping syndrome, 625
- in gastric surgery, 605, 611, 612, 616
- in hypertension, 250
- in hyperthyroidism, 730, 731
- in ileostomy, 660
- in infants, 192
- in jejunostomy, 614
- in malnutrition, 206, 605
- in nephritis, 259
- in obesity, 204
- in pyloric obstruction, 609
- in small bowel surgery, 643
- in thoracic surgery, 571, 579, 584, 590
- in ulcerative colitis, 657
- low cholesterol, in arterio-sclerosis, 765
- low-residue, 801
- postoperative, 124, 788
- reducing, 204
- regular, 71, 802
- relation to wound healing, 130
- semisolid, 801
- special, 801
- surgical liquid, 801
- soft, 801
- Dietary requirements, normal, 125
- Diethyl oxide (see Ether)
- Digestants in removal of wound slough, 487
- Digestion, carbohydrate, 50
- fat, 53
- protein, 60
- Digitaline Nativelle, 245

Digitalis, administration of, 244  
   in aged patient, 199  
   in auricular fibrillation, 237  
   in auricular flutter, 235  
   in cardiac disease, 232  
   in hypertension, 252  
   in paroxysmal tachycardia, 234  
   in thyrocardiac disease, 741  
   in thyroid crisis, 744, 748  
   indications for, 238  
   pharmacologic effects of, 243  
   toxic effects of, 238  
 Digitoxin, 245  
 Dihydratachysterol in hypoparathyroidism, 753  
 Diiodotyrosine, 739  
 Dilatation, acute gastric (see Stomach)  
 Dilaudid, 90, 118, 628  
 Diodrast for arteriography, 775  
 Direct blood transfusion, 174  
 Disease, associated, effects of hyperthyroidism on, 727  
   in aged patients, 198  
   in gastric disease, 601  
   in surgical patient, 104  
   undiagnosed, morphine contraindicated in, 90  
 Disruption of wound (see Wound, dehiscence of)  
 Distention, gastric, as cause of paroxysmal tachycardia, 234  
   intestinal, 324  
     as symptom of intestinal obstruction, 419, 420, 440, 444  
     conservative treatment of, 435  
     oxygen therapy in, 436, 806  
     relation to venous thrombosis, 381  
   postoperative, as cause of wound dehiscence, 500  
   prophylaxis of, 429  
 Diuresis in sulfonamide toxicity, 281, 286  
 Diuretic drugs in congestive heart failure, 241, 741  
   in nephritis, 260  
 Dizziness caused by sulfonamide drugs, 279, 285, 289  
 Douche, vaginal, preoperative, 782  
 Dover's powder, 88  
 Drain, anal, postoperative, 682, 687  
   choice of, in tissue infection, 756  
   effects of, 492, 493  
   indications for use of, 491, 492, 497, 649  
   pelvic, 792  
     as cause of urinary retention, 331

Drain—Cont'd  
   peritoneal, in acute appendicitis, 648, 649  
   protection of, 444, 558  
   record of, 788  
   removal of, 494, 757  
     after cholecystectomy, 710, 715  
     after thyroidectomy, 746  
   sump (see Sump drain)  
   types of, 491  
   vaginal, removal of, 788  
 Drainage, closed, in empyema, 552, 553, 562  
   influence of, on protein deficiency, 64, 523  
   intercostal, in decortication of lung, 562  
     in empyema, 553, 558, 561  
     in tension pneumothorax, 567, 568  
   in thoracic surgery, 576, 580, 582  
   of appendical abscess, 650  
   of common bile duct, 711  
   of gall bladder, 711  
   of hand infection, 756, 757  
   of infected gangrene, 764  
   of lung abscess, 588  
   of parotid abscess, 412  
   of pelvic abscess, 652  
   of soft tissue infection, 756, 757  
   of subphrenic space infection, 410  
   of thyroidectomy incision, 746  
   of wound infection, 498  
   open, in empyema, 557, 590  
   postural, 575, 584, 586, 590  
 Dressing, fixation of, 470  
   for burn, 526  
   for colostomy, 667, 671, 679  
   for ileostomy, 659  
   materials for, 468, 469  
   of burn, technique of, 526, 528  
   of wound, technique of, 459, 465, 469  
   pressure, for burns, 526, 528  
   for wounds, 465  
   tight, relation to wound healing, 458  
   type, relation to wound healing, 468  
   wet, after hemorrhoidectomy, 682  
     contraindicated in decubitus ulcer, 345  
   in gangrenous lesions, 471  
   in treatment of infection, 470  
   maceration due to, 471, 473  
   technique of application, 472  
   use of penicillin in, 482  
   streptomycin in, 482  
 Drop, Murphy, 35

- Drugs, antispasmodic, in peptic ulcer, 606  
 bronchodilating, with postural drainage, 576  
 dosage in children, 88  
 stimulant, with spinal anesthesia, 100
- Dumping syndrome, 624
- Duodenum, fistula of, postoperative, 619  
 ulcer of, complications of, 627  
   hemorrhage from, 627  
   perforation of, 630  
   treatment with aluminum gel, 605  
     with protein hydrolysate, 606  
     vagus resection for, 633
- Dysphagia after thyroidectomy, 747
- Dyspnea, acute paroxysmal, 241  
 after thoracic injury, 564  
 in acute dilatation of stomach, 451  
 in congestive heart failure, 239  
 in hemothorax, 569  
 in pulmonary atelectasis, 360  
   embolism, 402  
 in wet lung, 566  
 nocturnal, 230, 231, 237  
 oxygen therapy in, 566  
 paroxysmal, 241

## E

- Early ambulation, 129  
 after appendectomy, 647  
 after gastric surgery, 611  
 in aged patients, 200  
 in prophylaxis of atelectasis, 367  
   of pulmonary embolism, 404  
   relation to venous thrombosis, 386
- Edema, as cause of postoperative parathyroid tetany, 751  
 as sign of thrombophlebitis, 384  
 effect on Fishberg test, 257  
 following excess salt intake, 27, 31  
   fluid replacement therapy, 23, 66, 107  
 in congestive heart failure, 241  
 in gastrointestinal anastomosis, 66, 619  
 in intestinal anastomosis, 643  
 in kidney disease, 257  
 in nephritis, 254  
 in protein deficiency, 28, 63, 107, 205  
 nutritional, as cause of pyloric obstruction, 66  
 of bladder mucosa in urinary retention, 330

- Edema—Cont'd  
 of wound, 457  
 pulmonary, following fluid replacement therapy, 23, 31, 34, 374  
   in burns, 537  
   in heart failure, 241  
   in pulmonary embolism, 404  
   use of positive pressure oxygen in, 804
- Ehrlich, diazo reagent of, 696
- Elective surgery, contraindicated in anemia, 215  
 in acute respiratory tract infection, 107  
 in angina pectoris, 248  
 in cardiac failure, 239  
 in coronary disease, 230  
 in hypoproteinemia, 66  
 in malnutrition, 205  
 preparation for, 102
- Electrocardiography in coronary thrombosis, 247  
 in diagnosis of pulmonary embolism, 403  
   of quinidine toxicity, 234, 237  
   of tachycardia, 236  
 in hypertension, 253
- Electrolyte balance, disturbance of, 27  
 in acute dilatation of stomach, 452  
 in biliary tract drainage, 713  
 in carcinoma of colon, 662  
 in congenital hypertrophic pyloric stenosis, 22, 194  
 in diffuse peritonitis, 444  
 in duodenal fistula, 622  
 in enterostomy, 645  
 in gastric disease, 602  
 in gastroduodenal suction, 425  
 in ileostomy, 660  
 in intestinal obstruction, 417, 418  
   paralytic, 441  
 in vomiting, 190, 320  
 regulation of, 21, 29, 32  
 restoration of, 29, 425, 437, 660
- Elimination, postoperative, 126
- Embolism, arterial, sympathetic ganglionectomy in, 767  
 pulmonary, 377, 400  
   after gastric resection, 615  
   as symptom of venous thrombosis, 384  
   differential diagnosis of, 403  
   effects of, 403  
   factors predisposing to, 401  
   in gynecologic surgery, 790  
   in nonsurgical patients, 378

**Embolism, pulmonary**—Cont'd  
 mechanism of, 403  
 oxygen therapy in, 405, 805  
 pathogenesis of, 378, 380  
 preoperative, 791  
 prevention of, 401  
 symptoms of, 401  
 treatment of, 401

**Emergency operation, authorization**  
 for, 103  
 in acute appendicitis, 647, 649, 651  
 in anemia, 215  
 in children, 194  
 in complete obstruction of colon, 665  
 in diabetes, 266, 267  
 in impending shock, 144  
 in intestinal obstruction, 415, 417, 423, 424, 426, 437  
 in malnutrition, 205  
 in peptic ulcer hemorrhage, 627, 628  
 perforation, 630  
 in pregnancy, 227  
 preparation for, 110  
 prevention of shock in, 144

**Emotion, disturbed, as indication**  
 for preoperative medication, 83, 92  
 in child, 191  
 in hyperthyroidism, 726, 728  
 in postoperative period, 317  
 in preoperative period, 103, 131  
 relation to shock, 134

**Emotional factors in gynecology,**  
 779  
 in surgical patient, 83, 92, 103, 131  
 in stability, postoperative, 317  
 strain, as contributory cause of tachycardia, 231, 233

**Empyema, 550**  
 after hemothorax, 568, 570  
 after pneumonectomy, 580  
 after pulmonary lobectomy, 582, 590  
 after thoracoplasty, 595  
 cavity, obliteration of, 558, 560  
 chronic, causes of, 561  
 effects of, 551  
 closed drainage in, 553  
 complicated by pneumothorax, 552  
 encapsulated, 551  
 in pulmonary tuberculosis, 592  
 metapneumonic, 550  
 open drainage in, 557  
 progression of, 551  
 protein deficiency in, 64

**Empyema**—Cont'd  
 supportive treatment in, 560  
 synpneumonic, 550  
 treatment of, 552  
 by pulmonary decortication, 561  
 by rib resection, 558  
 by thoracentesis, 553  
 with penicillin, 300

**Encouragement, value of, 131**

**Endocrine system, role of, in hyperthyroidism, 724, 732**

**Endometriosis, 783**

**Enema, barium, 661, 662, 664, 804**  
 before anal surgery, 681, 682  
 before proctoscopy, 680  
 for administration of Avertin, 96  
 of chloral hydrate, 84  
 of paraldehyde, 84  
 glycerin and water, 326, 785  
 hydrogen peroxide, 127, 326  
 in diabetic coma, 268  
 in fecal impaction, 127  
 in intestinal distention, 127, 326  
 obstruction, 435, 441, 450  
 in urinary retention, 331  
 milk and molasses, 326  
 postoperative, 127, 646  
 avoided in colon anastomosis, 669  
 in bleeding peptic ulcer, 630  
 preoperative, 109  
 in colon surgery, 664  
 starch and opium, 657  
 tannic acid, 657  
 use of hydrogen peroxide in, 326

**Enteritis, regional, 641, 642**

**Enterokinase, 60**

**Enterostomy, care of, 643**  
 closure of, 646  
 disadvantages of, 645  
 dressing of, 645  
 feeding by, 644  
 in diffuse peritonitis, 450, 644  
 in intestinal obstruction, 439, 441

**Enterotomy in closure of colostomy, 673**

**Enzymes, digestive, in ileostomy drainage, 659**  
 gastric, in protein digestion, 60, 603  
 intestinal, in carbohydrate digestion, 51  
 in fat digestion, 54  
 in protein digestion, 61  
 pancreatic, in carbohydrate digestion, 51  
 in duodenal fistula drainage, 621

- Enzymes, pancreatic—Cont'd  
   in fat digestion, 54  
   in protein digestion, 60  
   protein content of, 58, 61  
   salivary, in carbohydrate digestion, 50
- Ephedrine, 100, 430  
   in shock, 144, 146, 155
- Epinephrine as hemostatic agent, 489  
   contraindicated in hypertension, 251  
   in allergic reactions, 185  
   in asthmatic bronchitis, 319  
   in serum reaction, 510  
   in shock, 145, 146  
   in transfusion reaction, 183, 184  
   not used with cyclopropane, 98  
   with postural drainage, 576
- Epithelium, digestion of, around ileostomy, 660  
   growth of, in burn, 520, 521, 540  
   in wound, 455, 456
- Erepsin in protein digestion, 61
- Ergosterol, irradiated, 211
- Eruetation following vagus resection, 624
- Erythroblastosis fetalis, 171
- Erythrocytes, changes in, in stored blood, 187  
   count, normal, 163  
   minimal preoperative, 143, 215  
   formation of bilirubin from, 693  
   fragility of, 187, 216  
   functions of, 24  
   in hemolytic anemia, 216  
   local application of, to wounds, 489  
   sickling tendency of, 217  
   transfusion of, 187
- Erythrol tetranitrate, 249
- Escherichia coli*, 281  
   as cause of diffuse peritonitis, 444  
   of septicemia, 354  
   effect of streptomycin on, 313  
   of sulfanilamide on, 282  
   of sulfasuxidine on, 294  
   of sulfathiazole on, 287  
   in burn infection, 538, 544  
   in subphrenic space infection, 408  
   in urinary tract infection, 340  
   in wound infection, 483, 486
- Eserine, 326
- Esmarch bandage, 776
- Essential hypertension, 249 (see also Hypertension)
- Estrogen, suppository, 783
- Ether, anesthesia, 99  
   contraindicated in diabetes, 270  
   in cardiac subjects, 238  
   as antiseptic, 461, 466, 478  
   in peripheral vascular disease, 767
- Ethylene, 98, 99  
   in diabetic patient, 270
- Eucupin, 683, 684
- Evaporation from body surface, 22
- Examination, physical (see Physical examination)  
   postoperative, 19  
   preoperative, 17, 104  
   in aged patient, 197  
   in child, 191  
   proctoscopic, 680
- Excretion of carbon dioxide, 23, 24, 25
- Exercise, apparatus for, 385  
   bed, postoperative, 116, 121, 129, 200, 385, 386  
   before thoracoplasty, 594  
   breathing, postoperative, 121, 200, 367, 385, 386  
   cardiac pain after, 230  
   disappearance of arrhythmia after, 253  
   in cardiac failure, 240  
   in hypertension, 251  
   in hyperthyroidism, 728  
   lack of, relation to venous thrombosis, 381, 385  
   passive vascular, 766  
   postural, 766  
   tolerance in cardiac disease, 230, 236
- Exhaled air, fluid loss in, 22
- Exophthalmic goiter (see Goiter, toxic diffuse)
- Exophthalmos, 724, 725
- Exploration in subphrenic space infection, 410
- Extracellular alkali, 23, 24
- Extrasystole, 232
- Extremity, amputation of, 768  
   closed, 772  
   gas gangrene in, 503, 505  
   guillotine, 769, 772  
   indications for, 764, 765  
   open, 772  
   skin traction in, 772  
   postoperative care in, 772  
   preoperative care in, 768  
   arterial pulsations in, 761  
   arteriovenous fistula of, 773  
   atrophic changes in, 761  
   examination of, 760  
   gangrene of, amputation for, 768  
   effect of wet dressings on, 471  
   infections of, 756

## Extremity—Cont'd

- occlusive arterial disease of, 758
  - diagnostic tests in, 761
  - examination in, 758
  - history in, 758
  - skin changes in, 759
  - treatment in, 763
- postural exercises in, 766
- refrigeration of, 769

- Exudate, peritoneal, in intestinal obstruction, 438
  - in perforative appendicitis, 648
  - in peritonitis, 442
- serous, as symptom of wound dehiscence, 500

## F

- Face, burns of, 531
- Factor, antianemic, storage of, in liver, 694
- Failure, cardiac, congestive, 236, 238, 239, 253, 404
  - in thyrocardiac disease, 229, 740
  - circulatory, in heart disease, 133
  - in shock, 133
  - peripheral vascular, in shock, 137, 138
- Faintness as symptom of pulmonary embolism, 381, 402
- False positive urinary sugar test, 84
- Family, notification of, 103
- Fascia, splitting of, in treatment of gas gangrene, 505
- Fat, absorption of, 54
  - as source of energy, 55, 57
  - content of diet in biliary tract disease, 56, 703
  - in diabetes, 263
  - in protein depletion, 71, 206
  - relation of, to absorption of vitamin A, 207
  - of vitamin K, 220, 705
  - of liver, 55, 67, 207, 702
- deficient absorption of, in bleeding tendency in jaundice, 220, 705
- deposition in liver, 55
  - effect of antilipotropic factors on, 56
  - of lipotropic factors on, 57, 207, 702
  - in chronic pancreatitis, 56
  - in diabetes, 56, 58
  - in dietary deficiency, 56, 206
  - in pregnancy, 56
- digestion of, 53, 694
- formation of, from carbohydrate, 55

## Fat, formation of—Cont'd

- from protein, 55, 693
- of ketones from, 57, 125, 693
- metabolism of, 53, 55, 693
  - as affected by biliary fistula, 57
  - in diabetes, 58
  - in starvation, 57, 125
  - relation to carbohydrate metabolism, 125
- oxidation of, 693
- Fear as contributory cause of shock, 131
- Fetal impaction, 127
- Feces, effects of streptomycin on, 296, 664
  - of sulfasuxaline on, 294, 664
  - of sulfathalidine on, 295, 664
- excretion of nitrogen in, 61
- fluid loss in, 22
- Feeding, postoperative, of infants, 195
- Femoral vein, ligation of, in venous thrombosis, 392
  - technique, 395
  - thrombosis of, 378, 379, 393
- Ferric ammonium citrate, 216
- chloride as hemostatic agent, 490
- Ferrous carbonate, 216
- sulfate, 216, 617
- Fever, albuminuria in, 256
  - as symptom of bronchopneumonia, 372
  - of dehydration, 123, 190
  - of gas gangrene, 504
  - of hyperthyroidism, 727, 743, 718
  - of infusion reaction, 43
  - of intestinal obstruction, 420, 423
  - of liver failure, 720
  - of lung abscess, 375, 376
  - of paralytic intestinal obstruction, 440
  - of pelvic abscess, 443, 651
  - of peritoneal abscess, 443, 650, 651
  - of peritonitis, 444, 651
  - of pharyngitis, 318
  - of postoperative parotitis, 411
  - of pulmonary atelectasis, 359, 363, 560
  - of pyelophlebitis, 652
  - of septicemia, 354
  - of subphrenic space infection, 409, 443, 651
  - of sulfonamide toxicity, 279, 285, 289, 291
  - of thiouracil toxicity, 733, 734
  - of thrombophlebitis, 384
  - of transfusion reaction, 183



Fever, as symptom—Cont'd  
 of urinary tract infection, 337  
 of venous thrombosis, 384  
 of wet lung, 566  
 of wound dehiscence, 500  
 infection, 497  
 in children, 190, 192  
 postoperative, 19  
 therapy, foreign protein, 766

Fiberglas as dressing for wound, 469

Fibrillation (*see* Auricular fibrillation)

Fibrin, foam, as hemostatic agent, 490  
 formation of, 63, 163

Fibrinogen, functions of, 62, 63, 163  
 plasma, 800  
 synthesis of, in liver, 694

Fibrous tissue, formation of, in wounds, 128, 455, 456  
 relation of vitamin C to, 130, 458

Fishberg test, 198, 257

Fissure of anus, 686

Fistula, 511 (*see also* Enterostomy)  
 anatomy of, 511, 512  
 anorectal, 513, 687  
 arteriovenous, 773 (*see also* Arteriovenous fistula)  
 biliary, 56, 513, 514, 716  
 as cause of hypoproteinemia, 707, 710  
 effect of, on hepatic metabolism, 56  
 bronchopleural, after pulmonary resection, 580, 582  
 in lung abscess, 589  
 in thoracic injury, 568  
 cecal, 511  
 cerebrospinal, 513  
 classification of, 511, 513  
 clinical course of, 514  
 conditions interfering with healing of, 514, 515  
 duodenal, postoperative, 621  
 external, 459, 511  
 fecal, 513, 514  
 diagnosis of, 513, 792  
 in appendical peritonitis, 651, 653  
 in gynecologic surgery, 791  
 healing of, 514  
 internal, 511  
 postoperative, in resection of rectum, 678  
 rectovaginal, postoperative care in, 788  
 preoperative care in, 783  
 rectovesical, 513

Fistula—Cont'd  
 relation to wound healing, 458, 599  
 salivary duct fistula, 513  
 small intestinal, 514  
 ureteral, postoperative, 676  
 ureterovaginal, 793  
 urethral, 513  
 urinary, identification of, 513, 793  
 vesicovaginal, 513, 792  
 postoperative care in, 794  
 preoperative care in, 794

Fixation of dressings, 460, 466, 470  
 relation of, to pulmonary atelectasis, 366

Flora (*see* Bacteriology)

Fluid balance (*see also* Fluid replacement therapy)  
 chart (*see* Chart, fluid balance)  
 disturbed, 21, 27  
 effect of, on wound healing, 457, 498, 500  
 in acute appendicitis, 647  
 gastric dilatation, 453  
 in aged patient, 21, 198  
 in anemia, 214  
 in burns, 523  
 in carcinoma of colon, 662  
 in chronic malnutrition, 28, 205  
 in congenital hypertrophic pyloric stenosis, 22, 194, 195  
 in diabetes, 262, 268, 270  
 in diarrhea, 34, 190  
 in duodenal fistula, 622  
 in emergency surgery, 110, 647  
 in enterostomy, 645  
 in gastrointestinal suction drainage, 21  
 tract disease, 21, 27, 601, 604  
 in hyperthyroidism, 727, 730  
 in hypoproteinemia, 63, 65, 69, 205  
 in ileostomy, 660  
 in infant, 21, 22, 190, 194  
 in intestinal obstruction, 417, 418, 420  
 in nephritis, 259  
 in obesity, 204  
 in peritonitis, 444  
 in postoperative period, 120, 122  
 in preoperative period, 102, 106  
 in pyloric obstruction, 602  
 in septicemia, 355  
 in sulfonamide toxicity, 280

**Fluid balance, disturbed—Cont'd**  
 in surgery of biliary tract, 717  
 in ulcerative colitis, 657  
 in uremia, 260  
 in vomiting, 22, 120, 190, 320  
 symptoms of, 27  
 urinary changes in, 28  
 maintenance of, 21, 23, 30, 32  
 postoperative, 122  
 relation of food intake to, 22  
 daily requirement of, 22, 78  
 deficiency, evidences of, 27  
 intake, 22, 30  
 excessive, 23  
 interstitial, 23  
 intracellular, 23  
 levels, intestinal, in obstruction,  
 421  
 loss, by evaporation, 22  
 from ileostomy, 660  
 in acute dilatation of stomach,  
 452  
 in diffuse peritonitis, 444  
 in exhaled air, 22  
 in feces, 22  
 in intestinal obstruction, 417,  
 418, 420  
 in regulation of body heat, 22  
 in shock, 135, 136, 137, 138  
 in sweat, 22  
 in urine, 22  
 output, 22, 30  
 plasma, 21  
 replacement therapy, amino acids  
 in, 69  
 by hypodermoclysis, 30, 36  
 by infusion, 30, 38, 41, 76,  
 812  
 by intramedullary adminis-  
 tration, 44  
 by intraperitoneal infusion,  
 44  
 by proctoclysis, 35  
 complications of, 34, 38, 43  
 during gastrointestinal suc-  
 tion drainage, 30, 324,  
 426  
 during operation, 111, 576,  
 607  
 edema caused by, 21, 107  
 effect of, on urinary output,  
 330  
 guide to, 123  
 in acidosis, 33  
 in acute appendicitis, 647  
 dilatation of stomach, 453  
 in aged patient, 198, 200  
 in alkalosis, 34  
 in biliary fistula, 30, 713  
 tract disease, 703, 709

**Fluid replacement therapy—Cont'd**  
 in bronchopneumonia, 374  
 in burns, 532, 534, 537, 538  
 in cardiac disease, 35, 239  
 in children, 33, 193, 195  
 in congenital hypertrophic  
 pyloric stenosis, 194  
 in congestive heart failure,  
 239, 240  
 in crush injury, 141  
 in dehydration, 66, 78  
 in diabetes, 265  
 in diabetic patient, 268, 270,  
 271  
 in duodenal fistula, 622  
 in emergency surgery, 110  
 in empyema, 560  
 in enterostomy, 645  
 in gastric surgery, 604, 609,  
 612, 616  
 in hypertensive patient, 251  
 in hyperthyroidism, 730, 731,  
 746  
 in hypoproteinemia, 63, 66,  
 106, 205  
 in ileostomy, 660  
 in intestinal obstruction, 420,  
 425, 437, 642  
 in kidney disease, 34, 259  
 in paralytic intestinal ob-  
 struction, 441  
 in perforated peptic ulcer,  
 630, 631  
 in peritonitis, 446, 447, 651  
 in postoperative vomiting,  
 120, 320  
 in prophylaxis of venous  
 thrombosis, 386  
 in pyloric obstruction, 609  
 in septicemia, 355  
 in shock, 145, 154, 156  
 in sulfonamide toxicity, 280  
 in tetanus, 510  
 in thyroid crisis, 743  
 in ulcerative colitis, 657  
 in uremia, 260  
 indications for, 27  
 methods of, 35  
 postoperative, 32, 122, 668,  
 672, 709, 746  
 preoperative, 106, 107, 108,  
 143  
 principles of, 29, 78  
 protein hydrolysate in, 69, 76  
 reactions following, 43  
 use of potassium in, 34  
 requirement in children, 193

**Fluoroscopy as and in passage of**  
 Miller-Abbott tube, 431  
 in hiccup, 343

- Flutter, mediastinal, 549  
 Folic acid, 218, 734  
 Food intake, relation to fluid balance, 22  
 Foot, burns of, 530  
   drop, postoperative, 116  
 Foreign body as cause of postoperative wound infection, 498  
   in chest wound, 564  
   relation to wound healing, 458, 498, 499  
 Fowler position, 114  
   contraindicated during anesthesia, 374  
   in diffuse peritonitis, 115, 447  
   in intestinal obstruction, 435  
   in tracheobronchial aspiration, 369  
   in urinary retention, 331  
   postoperative use of, 385  
   relation to venous thrombosis, 381  
 Fracture, compound, gas gangrene following, 503  
   tetanus following, 507  
 Fredet-Rammstedt operation, 22, 194  
 Fructose, metabolism in liver, 693  
 Function, hepatic (*see* Liver function)  
   kidney (*see* Kidney function)

## G

- Galactose, metabolism in liver, 693  
   tolerance test of liver function, 693, 702  
 Gall bladder (*see also* Biliary tract):  
   drainage of, 711  
   functions of, 695  
   visualization of, 698, 803  
 Ganglia, sympathetic, anesthetization of, in acute thrombophlebitis, 399, 400  
   in arteriovenous fistula, 776, 777  
   in occlusive arterial disease, 763, 767  
   block of, with tetraethyl ammonium chloride, in acute thrombophlebitis, 400  
   in occlusive arterial disease, 767  
 Ganglionectomy, sympathetic, in occlusive arterial disease, 763, 767, 776, 777  
 Gangrene, arteriosclerotic, diagnosis of, 760, 761  
   treatment of, 763, 764  
 Gangrene—Cont'd  
   diabetic, 267, 768  
   dry, 768  
   effect of wet dressings on, 471  
   gas (*see* Gas gangrene)  
   heat therapy contraindicated in, 117, 765  
   infected, 764, 768  
   of intestine in obstruction, 418, 421, 423, 438, 666  
   of lung in lung abscess, 375, 586  
   in tuberculosis, 591  
   of parotid gland, 411  
   refrigeration in, 769  
   wet, 768  
 Gargle in pharyngitis, 318  
 Gas bacillus antitoxin, use of, before amputation, 769  
   in burns, 539  
   in crushing injury, 141  
   polyvalent, 505, 506  
   infection, clinical types of, 503  
   in amputation of extremity, 503  
   in compound fracture, 503  
   in lacerated wound, 503  
   in peritonitis, 444, 503  
   sources of, 503  
 organisms, 503  
 gangrene, 503  
   commonest sites of, 504  
   cultures in, 505  
   diagnosis of, 504  
   diseases predisposing to, 503  
   prophylaxis of, 505  
   treatment of, 505, 506  
     with antitoxin, 506  
     with penicillin, 506, 507  
     with streptomycin, 506  
     with sulfonamide drugs, 506  
     with x-ray, 506, 507  
   intestinal, sources of, 324, 436  
   pains, as symptom of intestinal obstruction, 419, 424  
   postoperative, 127, 325  
 Gastrectomy (*see* Stomach)  
 Gastric (*see also* Stomach):  
   analysis, 603  
   dilatation (*see* Stomach)  
   discomfort, postoperative, 624  
   juice, composition of, 603  
     effect of histamine on secretion of, 603  
     of vagus nerve resection on secretion of, 633  
   secretion of, 633  
 lavage, 320  
   contraindicated in peptic ulcer hemorrhage, 628  
   perforation, 631  
   in acute dilatation of stomach, 452

## Gastric lavage—Cont'd

- in carcinoma of stomach, 608
- in cardiac disease, 239
- in diabetic coma, 268
- in hiccup, 342
- in paralytic intestinal obstruction, 441
- in paroxysmal tachycardia, 234
- in postoperative nausea, 320
- preoperative, in children, 194, 195
- in gastric surgery, 607
- in pyloric obstruction, 609, 610
- technique of, 320
- retention, 610
- suction apparatus, 322
  - as adapted for pleural drainage, 554, 556, 557
  - drainage (see Suction drainage, gastric)
- symptoms after vagus nerve resection, 634
- Gastroenterostomy combined with vagus nerve resection, 634
  - diet after, 611
  - postoperative orders in, 610
  - stomal obstruction after, 619
  - ulcer after, 626
- Gastrointestinal tract disease, anemia in, 214, 601, 604
  - associated disease in, 601
  - dehydration in, 21, 27, 601
  - protein deficiency in, 64, 601, 603
  - results of surgery in, 600, 601
  - surgical risk in, 600, 601
  - vitamin therapy in, 603
- series in gastric disease, 602
- in intestinal disease, 642
- preparation for, 803
- Gastrostomy, 637
  - feeding by, 638
  - permanent, 638
  - temporary, 637
- Gauze, absorbable, as hemostatic agent, 491
  - in posthemorrhoidectomy bleeding, 683
  - in postoperative incisional bleeding, 496
  - fine meshed, as drainage material, 491
  - in dressing of burns, 527, 542
  - of wounds, 468
- Gelatin in treatment of shock, 152, 156
  - sponge as hemostatic agent, 490, 496

- Gentian violet as tanning agent, 526
  - use of, in decubitus ulcer, 345
  - in septicemia, 356
- Globulin, plasma, 62, 65, 800
  - functions of, 62, 63
  - in albumin-globulin ratio, 62, 65
  - in hemophilia, 219
  - in malnutrition, 65
  - relation of, to antibodies, 63
- Glomeruli in glomerulonephritis, 254
- Glomerulonephritis, acute, 254
  - chronic, 254
- Glucose (see also Dextrose):
  - formation from amino acids, 693
  - from carbohydrate, 51
  - from fat, 51
  - from protein, 51, 52
  - metabolism of, 51
  - serum, 799
  - storage of, 51, 52
- Glutamic acid, 59
- Glycerine, local use of, in pruritus ani, 688
  - use of, in enema, 137, 326, 331
- Glycine, 59
- Glycogen depletion in hyperthyroidism, 730
  - in malnutrition, 206
  - in starvation, 55
  - ketosis in, 57
  - deposition, effect of insulin on, 53
  - hepatic, 53, 125, 702, 709
  - metabolism, of, 51, 52
  - reserve in diabetes, 263
  - restoration of, 106, 125, 709
  - synthesis of, 52
- Glycosuria after dextrose infusion, 38, 52, 270
  - in diabetes, 263, 264, 266, 268, 269, 271
- Goiter (see Thyroid)
- Grafting of skin (see Skin grafting)
- Gramicidin as antibiotic agent, 483
- Granulation tissue in healing of burn, 541, 542, 543
  - of wound, 456
- Granulocytopenia (see Agranulocytosis)
- Graves' disease (see Thyroid)
- Gridiron incision for carbuncle, 346
- Growth-stimulants in treatment of wounds, 488
- Guaicacel as expectorant, 319
- Gum acacia in treatment of shock, 152, 156
- Gynecologic surgery, 779
  - care in operating room, 783
  - choice of time for, 782
  - early ambulation in, 786

- Gynecologic surgery—Cont'd  
 postoperative care in, 784  
 complications in, 785, 789  
 diet in, 788  
 preoperative care in, 779  
 removal of drains after, 788  
 Rh blood type in, 781  
 thromboembolic disease in, 790  
 urinary retention following,  
   328, 787  
   tract infection in, 337, 782  
   use of estrogens in, 783  
   testosterone in, 783  
 Gynecology, history in, 779  
 physical examination in, 780

## H

- Habituation to barbiturate drugs, 85  
 to narcotic drugs, 87  
 Hand, burns of, 530  
 infections of, 756, 757  
 position of function of, 530  
 Hartmann's solution, 33  
 Headache after blood transfusion,  
   179, 183, 184  
   after use of barbiturates, 85  
   of chloral hydrate, 84  
   of vasodilator drugs, 249  
   in hypertension, 250  
   in penicillin therapy, 300  
   in streptomycin therapy, 314  
   in sulfonamide therapy, 279, 285,  
     289  
   in uremia, 260  
   oxygen therapy in, 806  
   sodium nicotinate in, 210  
 Head injury, morphine contrain-  
   dicated in, 90  
 Healing of amputation stump, 772  
   of burns, 519, 520, 541  
   of empyema cavity, 558  
   of fistula, 514  
   of wound, 127, 455, 456 (*see also*  
     Wound)  
   process, 127, 455  
 Heart (*see* Cardiac)  
 Heat, body, conservation of, 117  
   in children, 195  
   regulation of, 22, 122, 694  
   lamp after perineal surgery, 789  
   local, contraindicated in gangrene,  
     765  
   tent, 117  
   in abdominal distention, 326,  
     441, 450  
   in burns, 537  
   in occlusive arterial disease of  
     extremity, 117, 765  
 Hematemesis after gastric surgery,  
   617  
   after protracted vomiting, 320  
   from peptic ulcer, 627  
 Hematinics, use of, after gastric  
   resection, 617  
   in anemia, 215  
 Hematocrit after hemorrhage, 149  
   in blood volume deficit, 148  
   in burns, 522, 535, 538  
   as guide to therapy, 533, 537  
   in dehydration, 24  
   in shock, 142, 148, 149  
   as guide to therapy, 148, 162  
   preoperative, 105  
 Hematogenic shock, 136, 137  
 Hematoma, 496, 750  
   in venipuncture, 40  
 Hematopoiesis, depression of, 214  
 Hematuria, 256  
   in nephritis, 254, 256  
   in sulfonamide therapy, 280, 286,  
     289, 291, 339  
 Hemochromatosis, 694  
 Hemoclastic crisis, 216, 705  
 Hemoconcentration in burns, 522,  
   524, 532, 534  
   in dehydration, 27  
   in hypoproteinemia, 63, 69, 107  
   in shock, 149  
 Hemodilution after hemorrhage,  
   148, 149, 351  
   after plasma transfusion, 139, 147  
 Hemoglobin, functions of, 24  
   in anemia, 214  
   low, as contraindication to opera-  
     tion, 143, 163  
   normal values of, 163  
   preoperative determination of,  
     104  
 Hemoglobinuria in burns, 522, 535  
   in crush syndrome, 140  
   in sulfonamide therapy, 286  
   in transfusion reaction, 182, 187  
 Hemolysis in burns, 522, 535  
   in congenital hemolytic jaundice,  
     216, 705  
   in sulfonamide therapy, 279, 286,  
     289, 291  
   in transfusion reaction, 182  
   of conserved blood, 187  
 Hemolytic jaundice, 216, 695, 701,  
   705  
 Hemophilia, 164, 218, 226  
 Hemophilus *influenzae*, effect of  
   streptomycin on, 314  
 Hemoptysis, 571  
   in lung abscess, 376  
   in pulmonary embolism, 402

Hemorrhage as cause of anemia, 214, 601  
 of shock, 132, 133, 137, 139  
 as indication for blood transfusion, 159  
 blood dilution in, 148, 149, 351  
 capillary, in scurvy, 211, 226  
 in thrombocytopenic purpura, 224  
 collapse in, 351  
 concealed, 351  
 during anticoagulant therapy, 392, 790  
 during operation, 159  
 from lung abscess, 589  
 from peptic ulcer, 627  
 in child, 195  
 in gastric disease, 214, 601  
 in hemophilia, 218, 226  
 in jaundice, 212, 706, 710, 717  
 in prothrombin deficiency, 212  
 in purpura, 224, 226  
 in scurvy, 211, 218  
 incisional, 495  
 into intestinal tract, 351  
 into peritoneal cavity, 351  
 into thoracic cavity, 351, 563, 564, 565, 568, 581  
 into tissues, 351  
 petechial, 218  
 postoperative, 350, 495  
 as caused by prothrombin deficiency, 706, 710, 717  
 in abdominal perineal resection, 677  
 in amputation, 772  
 in arteriovenous fistula, 777  
 in biliary tract surgery, 717  
 in gastric surgery, 617  
 in gynecologic surgery, 789  
 in hemophilia, 219  
 in hemorrhoidectomy, 683  
 in hypertensive patients, 252  
 in thoracic surgery, 563, 581  
 in thyroidectomy, 750  
 protein deficiency after, 64  
 replacement therapy after, 68  
 treatment of, with blood substitutes, 159, 162  
 transfusion, 159, 161  
 with hemostatic agents, 459, 496  
 Hemorrhagic states, blood transfusion in, 161  
 following dicumarol therapy, 352  
 treatment of, 392  
 following heparin therapy, 392  
 treatment of, 225, 392

Hemorrhagic—Cont'd  
 tendency, 218  
 in hemophilia, 218, 226  
 in jaundice, 219, 226, 705  
 in newborn, 213  
 in prothrombin deficiency, 219, 226  
 relation of prothrombin concentration to, 706  
 treatment of, 706, 717  
 vitamin K in, 213, 706  
 preoperative diagnosis of, 105, 219, 220, 702  
 Hemorrhoidectomy, oil-soluble anesthetic in, 683  
 postoperative care in, 682  
 complications of, 683  
 preoperative care in, 681  
 Hemorrhoids as cause of anemia, 214  
 Hemostatic substances, local use of, 489, 496  
 Hemothorax, 564, 568  
 decortication in, 569  
 following thoracic surgery, 563  
 infected, 570  
 treatment of, 568  
 Heparin, administration of, continuous, 387  
 intermittent, 388  
 subcutaneous, 389  
 as cause of postoperative hemorrhage, 790  
 formation of, in liver, 694  
 overdose with, treatment of, 392  
 role of, in blood clotting, 163  
 tolerance test, 225, 382  
 use of, in arterial surgery, 777  
 in indirect blood transfusion, 174  
 in occlusive arterial disease, 767  
 in prevention of peritoneal adhesions, 416  
 in prophylaxis of arterial thrombosis, 777  
 of venous thrombosis, 387  
 in treatment of pulmonary embolism, 401  
 of venous thrombosis, 387  
 with dicumarol, 391  
 Hepatitis, prothrombin deficiency in, 707  
 thymol turbidity test in, 701  
 Hepatorenal syndrome, 720  
 Hernia, internal, of small intestine, 642  
 Herniation of intestine in wound disruption, 501  
 postoperative, 366

Hernioplasty, ventral, intubation in postoperative treatment of, 429

Hexylresorcinol, 338

Hiccough, 342  
in acute dilatation of stomach, 451

Hinton test in blood donor, 169

Hippuran for cholangiography, 714  
in diagnosis of fistula, 513

• Hippuric acid, synthesis of, in liver, 699  
test of liver function, 699, 702

Histamine, flare test, 762  
gastric response to, 603  
after vagus nerve resection, 633

Histidine, 59

Hoarseness after thyroidectomy, 748

Hoffman's anodyne in hiccough, 342

Hofmeister operation, 624

Homans' sign, 384

Hormone, anterior pituitary thyrotropic, 725, 726, 732  
pancreatic, lipotropic, 57  
thyroid (see Thyroid)

Hot-water bottles, use of, 117, 145

Hydrochloric acid in gastric juice, 603  
use of, in duodenal fistula, 621  
in gastric lavage, 608, 609

Hydrogen-ion concentration of blood, 25  
peroxide as antiseptic, 479  
as mouthwash, 202  
in dressing of wound, 347, 463, 466, 476  
in enema, 326

Hydrolysate (see Protein hydrolysate)

Hydroxyglutamic acid, 59

Hydroxyproline, 59

Hyperacidity in peptic ulcer, 603, 604

Hyperemia, intermittent venous, 766

Hyperglycemia, 52, 53  
in diabetes, 263, 265, 271

Hyperinsulinism, effects of, 53

Hypermetabolism, chronic protein deficiency, in 64

Hyperplasia, endometrial, 783

Hypertension, 249  
albuminuria in, 256  
as contraindication to Avertin, 97  
to Pitressin, 327  
to spinal anesthesia, 99  
associated with cardiac disease, 252, 253  
glomerulonephritis, 252, 255  
diet in, 250  
medication in, 251, 253

Hypertension—Cont'd  
postoperative complications in, 252, 254  
preoperative care in, 250  
shock in, 142, 143, 252  
surgical risk in, 250  
use of intravenous fluids in, 252

Hyperthyroidism, 724, 726  
auricular fibrillation in, 741  
cardiac disease in, 739 (see also Thyrocardiac disease)  
crisis in, 742, 747  
effects of, on associated disease, 267, 727  
on heart, 739  
etiology of, 724  
exophthalmos in, 725  
in diabetic patient, 267  
latent, 740  
mental state in, 728  
nodular goiter with, 724, 732, 735, 738  
physiologic effects of, 726, 742  
postoperative care in, 745  
complications in, 747  
preoperative care in, 728  
relief of toxicity in, 731, 737  
symptoms of, 726  
use of Avertin in, 96  
iodine in, 737, 738  
oxygen in, 743, 746  
propylthiouracil in, 736  
thiouracil in, 734

Hyperionus, muscular, in parathyroid tetany, 752  
in tetanus, 508

Hypertrophic pyloric stenosis (see Congenital hypertrophic pyloric stenosis)

Hypnotic drugs, 83

Hypocidity in gastric disease, 603, 604, 608

Hypochloremia, 32  
in ileostomy, 660

Hypodermoclysis, 36  
administration of sulfonamide drugs by, 282, 291  
in infants, 193, 194, 196

Hypoglycemia, 53, 272

Hypoglycemic shock, 265, 270, 271

Hypoparathyroidism (see Tetany, parathyroid)

Hypoproteinemia (see also Protein deficiency):  
albumin-globulin ratio in, 65  
as caused by enterostomy, 645  
decreased total blood volume in, 65  
dehydration in, 63  
edema in, 63

**Hypoproteinemia—Cont'd**

- effects of, 66, 205
  - fluid replacement therapy in, 63
  - in aged patient, 198
  - in diffuse peritonitis, 449
  - in gastric disease, 601
  - in hyperthyroidism, 731
  - in intestinal stomal obstruction, 66, 619, 643
  - in malnutrition, 28, 205
  - in ulcerative colitis, 657
  - increased tendency to shock in, 66
  - masked by dehydration, 78
  - postoperative complications in, 67
  - preoperative correction of, 106
  - pyloric obstruction in, 66, 609
  - relation to decubitus ulcer, 345
    - to delayed convalescence, 67
    - to loss of tissue protein, 63, 65
    - to wound healing, 67, 458, 499, 500
  - treatment by transfusion, 63
  - vitamin deficiency in, 67
- Hypoprothrombinemia (see also Prothrombin, deficiency of):**
- caused by dicumarol, 390
  - causes of, 707
  - in jaundice, 220, 705
- Hypotension, albuminuria in, 256**
- as contraindication to spinal anesthesia, 99
- Hypothyroidism as caused by thiouracil, 732, 735**
- as contraindication to Avertin, 97
  - hepatic changes in, 57

**I**

- Ice bags for relief of pain, 120**
  - in refrigeration anesthesia, 770
  - in thyroid crisis, 743
- Icteric index, 695, 704**
- Idiosyncrasy to barbiturates, 86**
  - to morphine, 89
- Ileocecal valve, function of, 665**
- Ileocolostomy in carcinoma of colon, 427, 664**
- Ileostomy, 656**
  - bag, Koenig-Rutzen, 659
  - drainage from, 658
  - dressing of, 658
  - for ulcerative colitis, 656, 658
  - postoperative care in, 658
  - preoperative care in, 657
  - protection of skin in, 659
- Ileum, obstruction of, 417**
  - perforation of, 444
- Ileus (see Obstruction, intestinal, paralytic)**
- Iliac veins, ligation of, 394**
  - thrombosis of, 379, 380, 381

- Incision, operative, relation to post-operative atelectasis, 365, 366**
  - postoperative disruption of, 499
  - healing of, 127, 455
  - hemorrhage from, 495
  - infection in, 496
  - pain in, 120
- Incompatibility of blood for transfusion, 165, 167, 168, 171**
  - reactions due to, 181
- Incontinence, overflow, urinary, 330, 787**
- Indications for blood transfusion, 159**
  - for drainage of wound, 491, 649
  - for fluid replacement therapy, 27
- Indirect blood transfusion, 175**
- Infant (see also Children).**
  - blood loss in, 159
  - care of wound in, 196
  - congenital hypertrophic pyloric stenosis in, 22, 194, 195
  - erythroblastosis fetalis in, 169, 170
  - ether anesthesia in, 99
  - hemorrhagic disease of, 213
  - hypodermoclysis in, 193, 194, 195, 196
  - intestinal distention in, 196
  - intramedullary infusion in, 44, 45
  - transfusion in, 44, 45
  - intraperitoneal transfusion in, 43
  - pediatrician's care in, 191
  - postoperative feeding in, 195
  - shock in, 195
  - problems in care of, 190
  - sedation in, 119, 196
  - venipuncture in, 195
- Infarction, pulmonary, 402**
- Infection as cause of anemia, 214**
  - of fistula, 511, 513
  - of thrombophlebitis, 394
- coincidental, in surgical patient, 107, 202**
- continued, in prolonged drainage, 493**
- decreased resistance to, 67, 205, 354**
- drainage in, 491, 756, 757**
- foci of, in septicemia, 354**
  - in surgical patient, 203
- in children, 190, 192**
- in diabetes, 266**
- in extremity, 756**
- in gangrenous extremity, 266, 764, 765, 768**
  - refrigeration in, 769
- in hematoma, 496**
- in hemothorax, 570**



**Infection—Cont'd**

- in incision, 497
- in thoracic surgery, 582, 583, 591
- in thoracoplasty, 594
- intermittent hyperemia contraindicated in, 766
- ischio-rectal, 689
- ketosis in, 58
- localization of, by heat, 470
- metastatic, 353
- near operative field, 109
- of amputation stump, 772
- of biliary tract, 692, 716
- of bronchial stump, 581, 582
- of extremity, 756
- of perineal wound, 677
- of subphrenic space, 406
- of urinary tract, 337
- of wound (*see* Wound)
- perianal, 689
- preoperative, of respiratory tract, 107, 192, 364
- prophylaxis of, 290
- relation of avitaminosis to, 207
- of hypoproteinemia to, 67, 205
- to venous thrombosis, 383
- to wound healing, 458, 499
- wound, treatment with local medication, 474
- with wet dressings, 470
- Infrared radiation, use of, in decubitus ulcer, 345
- Infusion (*see also* Fluid replacement therapy):
  - apparatus, Baxter, 812
  - Cutter, 823
  - Upjohn, 829
  - continuous, 40
  - effect of, on urinary output, 330
  - method of administration, 39
  - reaction after, 43
- Inguinal lymphatics, involvement of, in thrombophlebitis, 385
- Inhalation, aerosol, 585, 590
  - epinephrine, 319
  - medicated, 318
  - penicillin, 585, 590
  - steam, after thyroidectomy, 747, 751
  - in bronchitis, 319
  - in pulmonary atelectasis, 368
- Injury, crushing, as cause of shock, 140
  - predisposing to gas gangrene, 504
  - to tenes, 507
  - use of tourniquet in, 141, 769
- to extrahepatic bile ducts, 718, 719
- to parathyroid glands, 751

**Injury—Cont'd**

- to recurrent laryngeal nerve, 748
- to ureter, 792, 793
- Inositol, hypotropic effect of, 57
- Insensible loss of body fluid, 22, 122, 123
- Insomnia in hyperthyroidism, 745
  - in thyroid crisis, 743
  - postoperative, 119
  - preoperative, 108
- Instillation, bladder, 329, 333
- Insulin, effect on blood sugar 637
  - effectiveness decreased in infection, 266
  - in diabetic acidosis, 58
  - patient, 264, 265, 271
  - postoperative, 272
  - in nondiabetic patient, 53
  - overdosage, 272
  - physiologic effects of, 53
  - protamine zinc, 264, 272
  - regulation of dosage, 272
  - shock, 266, 271
  - test after vagus nerve resection, 636
- Intercostal artery, bleeding from, 564
  - nerve block, after thoracic surgery, 565, 578, 635
- Internal hernia 641
  - mammary artery, bleeding from, 564
- Internist, cooperation with, in surgery of cardiac patient, 229
  - of diabetic patient, 262
  - of tuberculosis, 592, 596
  - in thoracic surgery, 572
- Interstitial fluid, ionic concentration of, 23
- Interval appendectomy, 646
- Intestinal antiseptics, 293, 663
  - distention (*see* Distention, intestinal)
  - fistula (*see* Fistula)
  - gas, sources of, 324
  - obstruction (*see* Obstruction, intestinal)
- Intestine, absorption of carbohydrate from 38, 51
  - of fat from, 54
  - of protein from, 60
  - damaged, determination of viability of, 438
  - drainage of (*see* Suction drainage)
  - effect of operative trauma on, 324, 415, 416
  - large, operations on, 656, 661
  - postoperative paresis of, 324
  - preoperative cleansing of, 109
  - small, operations on, 641

- Intestine small—Cont'd  
 partial obstruction of, 641  
 surgical diseases of, 641  
   postoperative care in, 642  
   complications in, 643  
   preoperative care in, 642  
 trauma to, at operation, 791  
 wound infection of, after operations on, 663, 672, 674
- Intra-abdominal hemorrhage, diagnosis of, 351, 717  
 treatment of, 718
- Intracellular alkali, 23, 24  
 fluid, ionic concentration of, 23
- Intracranial disease as contraindication to Demerol, 91  
 use of morphine in, 90
- Intramedullary administration of blood, 44  
 of fluids, 44  
 of plasma, 46  
 oily fluids not suitable for, 47
- Intraperitoneal administration of blood, 43  
 of fluids, 44  
 of sulfonamide drugs, 284, 647
- Intrathoracic administration of penicillin, 301, 559, 562, 565, 569  
 of sulfonamide drugs, 559
- Intravenous anesthetics, 100
- Iodine as antiseptic, 461, 478  
 burns caused by, 478  
 content of blood, 737, 799  
 of thyroid gland, 737  
 fastness, 738  
 oral administration of, 737  
   contraindications to, 735  
   effects of, on thyroid gland, 738  
   in postoperative parotitis, 412  
   in thyrocardiac disease, 741  
   in thyroid crisis, 743  
   in toxic diffuse goiter, 731, 737, 738  
   nodular goiter, 738  
   indications for, 734, 737, 741  
   with propylthiouracil, 736, 737  
   with thiouracil, 736, 737  
 radioactive, 739
- Iodized oil in bronchography, 573, 584  
 in cholangiography, 714  
 in diagnosis of fistula, 513
- Ion, bicarbonate, 24  
 chloride, 24, 25, 26, 28, 30  
 hydrogen, 26  
 potassium, 23
- Ion potassium—Cont'd  
 loss of, in infantile diarrhea 33  
 shift of, in stored blood, 187  
 sodium, 23, 26, 28, 31
- Ionic concentration in body cells 23  
 fluids, 23
- Iprat, 85
- Iron in treatment of anemia, 215  
 of postgastrectomy anemia, 626  
 storage of, in liver, 694
- Irradiated ergosterol, 211
- Irradiation of skin lesions, 345
- Irrigation of colostomy, 667, 678, 679  
 of empyema cavity, 557, 558  
 of infected wounds, 474, 475, 677  
 of kidney pelvis in sulfonamide anuria, 281  
 of perineum in urinary retention, 331  
 of urinary bladder, 334, 335, 336
- Ischemia, influence of, on wound healing, 457  
 of kidney in crush syndrome, 140, 141  
 in shock, 137, 140  
 of viscera in shock, 137
- Ischemic neuritis, 758, 763
- Ischiorectal abscess, 689
- Isoagglutinins, 165
- Isoleucine, 59
- Isotopes, radioactive, 739
- J
- Jaundice (see also Bile, Biliary tract, Hemorrhagic Tendency, Liver, Prothrombin deficiency):  
 after transfusion reaction, 182  
   with conserved blood, 187  
 after use of sulfonamide drugs, 279, 286  
 cholecystography contraindicated in, 699, 703  
 examination of blood in, 695, 696, 702, 704  
   of stool in, 695, 704  
   of urine in, 695, 704  
 hemolytic, 695, 704, 705  
   acute crisis in, 705  
 hemorrhagic tendency in, 212, 219, 226, 704, 705, 708, 710  
 hypoprothrombinemia in (see Hemorrhagic tendency)  
 icteric index in, 695, 704  
 impairment of liver function in, 704  
 in gas bacillus infection, 505  
 in thyroid crisis, 743

**Jaundice—Cont'd**

laboratory tests in, 219, 695, 704  
 obstructive, 695, 704  
 postoperative, from injury to extrahepatic bile ducts, 719

hemorrhage in, 710  
 preoperative care in, 695, 704, 708  
 prothrombin deficiency in (see Hemorrhagic tendency)

serum alkaline phosphatase in, 697

bilirubin in, 697, 704

toxic, 695, 704

types of, 695, 704

use of carbohydrate in, 704

van den Bergh test in, 696, 704

vitamin A deficiency in, 208

K deficiency in (see Hemorrhagic tendency)

Jejunostomy, feeding by, 614, 622  
 for preoperative feeding, 608

in duodenal fistula, 621

nonoperative, 613

Jejunum, obstruction of, 417, 418

Jubé transfusion apparatus, 174

Jugular vein, ligation of, in lateral sinus thrombosis, 355

**K**

Kahn test of blood donor, 169

Kangaroo tendon in postoperative wound dehiscence, 501

Kaolin as protective skin dressing, 659

Karell diet, 240

Ketogenic diet, 338

Ketones, formation of, 57

in acidosis, 28, 29, 59

in diabetes, 28, 58, 266

Ketonuria, 29, 266, 320

Ketosis, 57, 125

treatment of, 33, 126

Kidney, arteriosclerosis of, 253

colic, intestinal distention in, 441

damage as contraindication to Avertin, 97

to barbiturates, 86

due to ischemia, 140, 141

to transfusion reaction, 182

in burns, 522, 574

in crush syndrome, 140, 141

in glomerulonephritis, 254

in hypertension, 250

in shock, 137, 140, 523

in sulfonamide toxicity, 280, 281, 289, 291, 292

in transfusion reaction, 182

preoperative care in, 255

**Kidney—Cont'd**

decapsulation, in treatment of anuria, 261, 281

disease, albuminuria in, 256  
 as contraindication to Avertin, 97

to sodium pentothal, 101

associated with biliary tract disease, 692, 693

effect of, on blood chemistry, 258

fluid replacement therapy in, 34, 35, 124

hypertension associated with, 255

mercurial diuretics contraindicated in, 241, 253, 260

preoperative care in, 259

uremia in, 260

use of barbiturates in, 86

diseases of, 253

effect of hypertonic sugar solution on, 34, 35

of sulfonamide drugs on, 280, 281, 289

elimination of sulfadiazine by, 292

of sulfathiazole by, 291

of sulfonamide drugs, by, 278, 280

excretion of sodium chloride by, 27, 31

failure in liver death, 720, 721

in nephritis, 254

postoperative, 199

function, 26, 27, 253

in hypertension, 249, 250

investigation of, 257, 692

postoperative depression of, 31  
 regulation of acid-base balance by, 23, 26

of electrolyte balance by, 26, 27, 31

stimulation of, 34, 184, 261

tests of, 256, 257

reserve capacity of, 254

toxic effects of sulfonamide drugs on, 280, 289, 291

Kimpton-Brown transfusion apparatus, 174

Kinked loops, intestinal, 418

Knee-chest position for sigmoidoscopy, 680

Koenig-Rutzen ileostomy bag, 659

Kupffer cells, 693

**L**

Laboratory studies in delayed wound healing, 499

in duodenal fistula, 622

in gastric surgery, 602

in hyperthyroidism, 728

- Laboratory studies—Cont'd  
 in ileostomy, 660  
 in ulcerative colitis, 657  
 test (see also special tests)  
 after vagus nerve resection, 636  
 for capillary fragility, 218  
 for prothrombin deficiency, 221  
 for sickle-cell anemia, 217  
 in jaundice, 695, 704  
 in sulfonamide therapy, 279  
 in thrombocytopenic purpura, 225, 226  
 preoperative, 104, 105  
 to determine liver damage, 697, 702
- Laceration of chest wall, 564  
 of lung, 564
- Lactate, sodium (see Sodium lactate)
- Lactic acid, 25  
 in carbohydrate metabolism, 52, 693
- Lanatoside-C (see Cedilanid)
- Large bowel (see Colon, Rectum, Anus)
- Laryngeal nerves, post-thyroidectomy paralysis of, 748
- Larynx, preoperative examination of, in thyroid disease, 729  
 reconstruction of, 749
- Latent edema, 31  
 hyperthyroidism, 233, 740  
 shock, 144  
 syphilis, 104, 105  
 tuberculosis, 104
- Lateral sinus thrombosis, 355
- Laudanum, 88
- Lavage, gastric (see Gastric lavage)
- Lecithin, 55, 56  
 in bile, 694  
 hypotonic effect of, 57
- Legal authorization for operation, 103
- Leucine, 59
- Leucopenia in propylthiouracil therapy, 736  
 in septicemia, 354  
 in sulfonamide therapy, 279, 286, 289  
 in thiouracil therapy, 733, 734
- Leucorrhea, treatment of, 782
- Levin tube for gastric lavage, 321  
 preoperative introduction of, 325
- Ligation, quadruple, in arteriovenous fistula, 776, 777  
 of bleeding vessel in postoperative hemorrhage, 352, 495, 718, 750, 790
- Ligation—Cont'd  
 of femoral veins in venous thrombosis, 387, 392, 395, 791  
 of iliac veins, 394  
 of jugular vein in lateral sinus thrombosis, 355  
 of regional vein, in septicemia, 354  
 of vena cava, 355, 394
- Linen as burn dressing, 530  
 as dressing in wounds, 469
- Lipase, activation of, by bile, 54, 694  
 in digestion of fat, 54
- Lipiodol (see also iodized oil)  
 in diagnosis of fistula, 513
- Lipocaine, lipotropic effect of, 57
- Lipoids, occurrence of, 55
- Lipotropic substances, 56
- Liver, abscesses of, in pyelophlebitis, 652  
 carcinoma of, 697, 707  
 cirrhosis of, 64, 703  
 damage as contraindication to Avertin, 97  
 to barbiturates, 86  
 to sodium pentothal, 101  
 bleeding tendency in, 707  
 caused by gum acacia, 152  
 by sulfonamide therapy, 286  
 by tannic acid, 522, 526  
 correction of, 207, 703  
 determination of, by laboratory tests, 697, 702  
 in burns, 522, 524  
 in chronic biliary tract disease, 692, 693  
 in jaundice, 704  
 in malnutrition, 55, 206, 702  
 physiologic changes in, 702  
 prothrombin deficiency in, 707  
 use of oxygen in, 710, 805  
 vitamin K deficiency in, 707
- death, 720
- dullness in subphrenic space in infection, 409
- extract in agranulocytosis, 734  
 in pernicious anemia, 214, 218  
 in postgastrectomy anemia, 626  
 in ulcerative colitis, 638
- failure, 720  
 after biliary tract surgery, 720  
 after gastric surgery, 624  
 in thyroid crisis, 727, 743
- fat content of, 55, 56
- function after biliary tract surgery, 711, 712  
 depression of, by gum acacia, 152  
 by pectin, 153

## Liver function—Cont'd

- effect of protein deficiency on, 67
  - impairment of, 56, 693, 704
  - improvement of, 702
  - in jaundice, 704
  - preoperative restoration of, 56, 702, 708
  - reserve capacity of, 693
  - tests, 697
    - bromsulfalein, 697, 702
    - cephalin-cholesterol flocculation, 701, 702
    - galactose tolerance, 698, 702
    - prothrombin synthesis, 701
    - Quick, 699, 702
    - rose bengal, 697, 702
    - tetraiodophenolphthaleïn, 698
    - thymol turbidity, 701
  - functions of, 693
    - body heat regulation, 694
    - detoxication, 694
    - excretory, 694
    - formation of ketones in, 57
    - metabolism of carbohydrate, 51, 693
      - of fat, 55, 693
      - of protein, 693
    - phagocytosis, 694
    - storage of antianemic factor, 694
    - of iron, 694
    - synthesis of aminoacetic acid, 699
      - of heparin, 694
      - of hippuric acid, 699
      - of plasma proteins, 62, 694
      - of prothrombin, 694, 707
      - of vitamin A, 694
  - glycogen content of, 53, 78, 125, 702
  - neoplastic disease of, serum alkaline phosphatase in, 697
  - susceptibility to damage, 55
  - weight of, 52
- Lividity in postoperative hemorrhage, 351
- Lobectomy, pulmonary (*see* Lung, resection of)
- Local anesthesia, 95
- Localized peritonitis (*see* Peritonitis)
- Loop, intestinal, closed, 418, 419, 420, 426
- Lordosis, albuminuria in, 256
- Lugol's solution, 739, 743 (*see also* Iodine, oral)
- in postoperative parotitis, 412
- Luminal, 83 (*see also* Phenobarbital)

## Lung, abscess of, 375, 586

- artificial pneumothorax contraindicated in, 574, 586
  - aspiration contraindicated in, 574, 587
  - bronchoscopy in, 586
  - complications of, 587
  - diagnosis of, 375
  - etiology of, 375
  - lobectomy for, 589
  - localization of, 587
  - pathology of, 375, 586, 591
  - pneumotomy for, 587, 588
  - postoperative care in, 588, 590
    - complications in, 589, 591
  - postural drainage in, 575, 586, 590
  - preoperative care in, 590
  - symptoms of, 375, 586
  - treatment of, conservative, 376, 587
    - surgical, 587, 588, 589
  - alveolar damage of, as caused by anoxia, 567
  - carcinoma of, diagnosis of, 574
  - inoperable, 574
  - pneumonectomy for, 581
  - disease of, diagnostic aspiration in, 574, 587
  - edema of, following thoracic surgery, 579
  - treatment with oxygen, 567, 805
  - fibrosis of, following bronchiectasis, 583
    - empyema, 551
    - lung abscess, 587
  - gangrene of, 374, 375
  - resection of, for bronchiectasis, 583
    - for lung abscess, 589
    - for suppurative disease, 583
    - for tuberculosis, 595
  - postoperative care in, 581, 586, 590
    - complications in, 582
  - tuberculosis of, 591
    - cavity formation in, 591
    - empyema in, 592
    - hemorrhage in, 592
    - pulmonary resection for, 595
    - surgical treatment of, 592, 595
    - thoracoplasty for, 592
    - wet, 566
- Lymphatic involvement in thrombophlebitis, 385
- Lysine, 59
- M
- Magnesium sulfate as wet dressing, 471
- Malaria, anemia in, 214

- Malignant disease** (*see also* special headings).  
 anemia in, 214  
 as cause of fistula, 513, 514  
 depression of hematopoiesis by, 214  
 relation of, to wound healing, 457, 500
- Malnutrition**, 205 (*see also* Hypoproteinemia)  
 anemia in, 28, 163  
 as cause of debility, 205  
 of stomal obstruction, 619  
 as indication for blood transfusion 163, 205  
 decreased blood volume in, 65  
 dehydration in, 65, 106, 143, 205  
 effect of, on convalescence, 67  
 hypoproteinemia in, 28, 34, 205  
 in burns, 545  
 in carcinoma of colon, 662  
 in children, 193, 194  
 in gastric disease, 601  
 in gynecologic patients, 779  
 in ulcerative colitis, 657  
 liver damage in, 206  
 postoperative, 64  
 preoperative care in, 106  
 prophylaxis of shock in, 143  
 relation of, to postoperative venous thrombosis, 383  
 treatment of, 34, 106, 143, 206
- Mandelic acid**, 338, 340
- Marginal ulcer**, postgastroctomy, 626
- Mask, oxygen**, 809
- Massive collapse of lung** (*see* Atelectasis, pulmonary)
- Matas compressor**, 776
- Matas-Moszkowicz test**, 776
- McBurney incision**, 746
- Meat content of diet in hypertension**, 251
- Mecholyl**, contraindications to use of, 235, 331  
 in paroxysmal tachycardia, 234  
 in urinary retention, 331
- Mediastinal flutter**, 549  
 shift after pneumonectomy, 579  
 after thoracic surgery, 580  
 in hemothorax, 565  
 in pulmonary atelectasis, 360  
 in tension pneumothorax, 549, 565
- Mediastinitis** following intramedullary administration of fluids, 48  
 thyroidectomy, 751
- Mediastinum**, extension of goiter to, 729  
 fixation of, 519
- Mediastinum**—Cont'd  
 shift of (*see* Mediastinal shift)  
 trauma to, 564
- Medical disease** simulating surgical condition, 110
- Medication**, hypnotic, 83  
 postoperative, 118  
 preoperative, 92, 108  
 sedative, 83
- Melena**, 351, 657, 661, 680
- Menadione** (*see also* Vitamin K):  
 administration of, 706, 710, 717  
 in treatment of dicumarol overdose, 392
- Menometrorrhagia**, use of testosterone in, 783
- Menorrhagia** as cause of anemia, 215
- Mental confusion** caused by barbiturate drugs, 861  
 by bromide intoxication, 83  
 by phenobarbital, 83, 85  
 depression in sulfonamide therapy, 279, 285  
 pulse rate in, 233
- Menthol**, use of, in steam inhalation, 318
- Mercurhydrin**, 241
- Mercupurin**, 241
- Mercurial diuretic drugs**, 241  
 contraindicated in presence of renal damage, 214, 253, 260
- Mercuric chloride** as vaginal douche, 782
- Mercurochrome** as antiseptic, 478  
 as urinary bladder instillation, 329, 333  
 use of, in septicemia, 356
- Merthiolate** as antiseptic, 478  
 as urinary bladder instillation, 333
- Mesenteric artery**, superior, 452
- Mesentery**, closure of, in colostomy, 672, 673  
 traction on, at operation, 416
- Metabolic acids**, 25, 26, 28, 693  
 disease (*see also* Diabetes, Thyroid disease, etc.):  
 effect of, on wound healing, 130, 457, 499  
 in surgical patient, 106, 203  
 prophylaxis of shock in, 143  
 disturbances, postoperative, 21, 125, 320
- rate**, determination of, in hyperthyroidism, 728, 729, 743  
 effect of iodine on, 738  
 of thiouracil on, 732, 737  
 in children, 195  
 in thyrocardiac disease, 741

- Metabolism, calcium, 212, 752  
 carbohydrate, 50, 51, 125, 126,  
     209, 210, 693  
 fat, 53, 55, 126, 693  
 glucose, 51, 693  
 glycogen, 52, 125  
 phosphorus, 212, 752  
 protein, 58, 61, 126, 693  
 Metaphen as anti-septic, 478  
 Metastases in carcinoma of colon,  
     661  
     of lung, 575  
 Metastatic abscesses, 353  
 Methedrine, 100, 144, 155  
 Methemoglobin in cyanosis, 286, 804  
 Methenamine, 338, 341  
     mandelate, 341  
 Methionine, 59  
     lipotropic effect of, 57  
     use of, in liver damage, 703  
 Methylene blue in identification of  
     urinary fistula, 513, 793  
     in localization of lung abscess,  
     588  
 Metrazol, 87  
 Michel clips, 463  
 Microaerophilic wound infection,  
     486  
 Migraine, 210, 806  
 Mikulicz operation for carcinoma  
     of colon, 662  
 Milk, postoperative restriction of,  
     125  
     protein concentrates in protein  
     replacement therapy,  
     72, 605  
     skim (see Skim milk)  
 Miller-Abbott tube, construction of,  
     430  
     contraindications to use of, 429,  
     437  
     following repair of ventral  
     hernia, 429  
     gastric distention during use  
     of, 434  
     in appendical abscess, 650  
     in diffuse peritonitis, 447, 450  
     in complete intestinal obstruc-  
     tion, 429, 436, 437  
     in gynecologic surgery, 785  
     in incomplete intestinal ob-  
     struction, 427  
     in mechanical intestinal ob-  
     struction, 429, 436, 612  
     in paralytic intestinal obstruc-  
     tion, 441  
     in postoperative wound de-  
     hiscence, 502  
     in preoperative preparation,  
     427, 436  
 Miller-Abbott tube—Cont'd  
     in prophylaxis of intestinal  
     distention, 429  
     obstruction, 427  
     of wound dehiscence, 429  
     in surgery of colon, 427, 664,  
     668, 669, 671  
     indications for use of, 427, 436  
     special types of, 432  
     technique of introduction of,  
     430  
     use of barium with, 434  
     withdrawal of, 435  
 Mineral oil, use of, after gynecologic  
     surgery, 329  
     after hemorrhoidectomy, 682  
     contraindicated, in colo-  
     rectomy, 679  
 Mitral stenosis, 238  
 Monckeberg's sclerosis, 761, 762  
 Morbidity, relation of extremes of  
     age to, 190  
 Morphine as aid in passage of Miller-  
     Abbott tube, 430, 431  
     as cause of vomiting, 89, 94  
     as peristaltic stimulant, 441  
     contraindicated in asthma, 319  
     in postoperative atelectasis, 368  
     contraindications to use of, 89  
     93, 319, 368  
     effect of, on intestine, 94, 326, 441  
     on urinary bladder, 94, 328  
     idiosyncrasy to, 89  
     in aged patient, 200  
     in biliary colic, 707  
     in blood transfusion reaction, 184  
     in burns, 525, 527, 532  
     in children, 88, 94, 119  
     in congestive heart failure, 210  
     in coronary thrombosis, 247  
     in diffuse peritonitis, 447, 450  
     in dressing of wounds, 494  
     in hypertension, 253  
     in neurosurgery, 90, 94  
     in paroxysmal dyspnea, 242  
     in peptic ulcer hemorrhage, 628  
     in perforated peptic ulcer, 630,  
     631  
     in postoperative hemorrhage, 353  
     in preoperative medication, 93, 94  
     in shock, 145, 156  
     danger of, 95, 532  
     in thyroid crisis, 743  
     indications for, 89  
     intravenous use of, 95, 532  
     overdosage with, 90  
     physiologic effects of, 89, 94  
     postoperative use of, 118, 610,  
     745, 784

Morphine—Cont'd  
 preoperative use of, 93  
 properties of, 88  
 Mortality in bleeding peptic ulcer,  
   627, 629  
   in Fredet-Rammstedt operation,  
     22, 194  
   in gastric resection, 600, 601  
   in intestinal obstruction, 415, 424  
   in liver failure, 720  
   in parotitis, 410  
   in peptic ulcer hemorrhage, 627  
   in perforating peptic ulcer, 630,  
     632  
   in pneumonectomy for carcinoma,  
     581  
   in pulmonary embolism, 378, 400  
     resection for bronchiectasis, 583  
     for lung abscess, 589  
     for tuberculosis, 596  
   in surgery complicated by cardiac  
     disease, 229, 230, 231,  
       232, 233, 234, 236,  
       237, 246, 247, 248  
     by diabetes, 262  
     by hypertension, 250  
     by nephritis, 254  
     by pregnancy, 227  
     of aged patient, 197  
     of colon, 636, 667  
     of infant, 190  
   in thoracoplasty, 593  
   in thyroid crisis, 743  
 Mosenthal test, 257  
 Mouth, infection of, in surgical  
   patient, 202  
 Mucin in gastric juice, 603  
 Murmurs, cardiac, 230, 231, 249  
 Murphy drip, 35  
 Muscle, appearance of, in gas gan-  
   grene, 504, 505  
   crushing injury of, as cause of  
     shock, 140  
   metabolism in, 52  
 Muscular atrophy in occlusive ar-  
   terial disease, 761  
 Myocardium, anoxemia of, in shock,  
   133  
   effect of hyperthyroidism on, 739  
 Myohemoglobin in crush injury,  
   140, 141

## N

Naphthoquinone derivatives (see  
 Vitamin K)  
 Narcotic drugs, 87  
   use of, in children, 119  
 Nasopharynx, irritation of, by  
   Miller-Abbott tube,  
   435

National Research Council, recom-  
 mendations on peni-  
 cillin, 298  
   study of streptomycin, 306  
 Nausea (see also Vomiting).  
   caused by bromide intoxication,  
     83  
   by chloral hydrate, 84  
   by mandelic acid, 341  
   by morphine, 785  
   by streptomycin, 314  
   by sulfonamide drugs, 279, 285,  
     289  
   during blood transfusion, 182  
   postoperative, 120, 125, 320, 720,  
     785  
 Nebulizer for epinephrine inhala-  
   tion, 319  
 Neck, postoperative sprain of, 112  
 Necrosis (see also Gangrene)  
   of burned tissue, débridement of,  
     527, 541, 542  
   of colon, exteriorized, in colos-  
     tomy, 671  
   in obstruction, 666  
   postoperative, 669  
   of intestinal septum in spur colos-  
     tomy, 672  
   of liver caused by tannic acid, 526  
   in burns, 522  
   in liver failure, 721  
   of renal tubular epithelium in  
     burns, 523  
   in crush syndrome, 140,  
     141  
   in liver failure, 721  
   in shock, 140, 523  
   in sulfonamide toxicity,  
     280  
   in transfusion reaction, 183  
 Needles for intramedullary trans-  
   fusion, 44, 46  
 Negative pressure, intrathoracic, in  
   normal respiration, 548  
   in suction drainage of em-  
     pyema, 554, 555  
   postoperative, 580, 581,  
     582  
   reduction of, in sucking  
     wound, 548  
   in tension pneumothorax,  
     549, 567  
 Negro, sickle-cell anemia in, 217,  
   249  
 Nembutal, 85, 93, 96, 232  
 Neosphenamine, use of, in aspira-  
   tion pneumonia, 375  
 Neo-iopax for arteriography, 775  
 Neonatal, 85  
 Neosynphrine, 100  
   as nasal decongestant, 430



- Neosynephrine—Cont'd  
   contraindication to, 98  
   in shock, 145, 146, 155
- Nephritis, 253
- Nephrostomy, 793
- Nerve, cutaneous, division of, in  
   occlusive arterial dis-  
   ease, 768  
   inferior laryngeal, effect of goiter  
     on, 729  
     injury to, 748  
     repair of, 749
- Nervous system, diseases of, as con-  
   traindication to spinal  
   anesthesia, 99
- Neuritis in vitamin B deficiency, 209  
   ischemic, 758, 763, 764
- Neurogenic shock, 134, 137
- Neurosurgery, preoperative medica-  
   tion in, 94  
   use of Avertin in, 96  
   of gelatin sponge in, 490
- Neurosyphilis, 104
- Neutropenia (*see* Leucopenia)
- Newborn, erythroblastosis in, 171  
   vitamin K therapy in, 213
- Nicoladoni-Branham sign, 774
- Nicotinic acid (vitamin B<sub>3</sub>), 209  
   in burns, 546  
   requirement during convales-  
   cence, 80
- Nitrazine test paper, 341
- Nitrites, use of, in angina pectoris,  
   248  
   in biliary colic, 707
- Nitrofurazone in treatment of  
   wound infection, 345,  
   347, 483, 688, 768
- Nitrogen balance, 62  
   maintenance of, 78  
   negative, 62, 63  
   positive, 62, 64  
   blood (*see* Nonprotein nitrogen)  
   excretion of, 61, 62, 65  
   in burns, 523, 545  
   in intestinal gas, 436, 806
- Nitroglycerin, use of, in angina pec-  
   toris, 248  
   in biliary colic, 707  
   drainage, 714, 715
- Nitrous oxide, 98, 99
- Nocturia in hypertension, 250
- Nocturnal dyspnea, 230, 250
- Nodular goiter (*see* Thyroid)
- Nonprotein nitrogen, blood, 258,  
   260, 799  
   in burns, 523  
   in dehydration, 29  
   in diffuse peritonitis, 449  
   in hypertension, 250
- Nonprotein nitrogen, blood—Cont'd  
   in intestinal obstruction, 417  
   in nephritis, 255, 258  
   in uremia, 260
- Norleucine, 59
- Normal salt solution (*see also* Fluid  
   replacement therapy)  
   as gargle, 318  
   as irrigation before cholangi-  
   ography, 714  
   as vaginal douche, 782  
   as wet dressing, 471  
   as wound irrigation, 475, 677  
   by hypodermoclysis, 30, 36,  
     38, 193  
   by infusion, 30, 31, 38  
   by proctoclysis, 35  
   daily intake of, 30, 78  
   during operation, 111  
   edema following use of, 31,  
     34, 124  
   excessive administration of,  
     31, 34, 124  
   in acidosis, 26, 33, 110, 266,  
     268  
   in acute dilatation of stom-  
     ach, 453  
   in alkalosis, 26, 34  
   in blood transfusion, 181  
   in burns, 534, 538  
   in children, 193, 195  
   in congenital hypertrophic  
     pyloric stenosis, 194  
   in diabetic acidosis, 266, 268,  
     269  
   in diffuse peritonitis, 448  
   in dressing of wound, 463, 466  
   in duodenal fistula, 623  
   in emergency operation, 110,  
     647  
   in enterostomy, 645  
   in gastric lavage, 607, 608,  
     609  
   in hypochloremia, 32  
   in ileostomy, 660  
   in infants, 38, 193, 194  
   in intestinal obstruction, 425  
   in replacement of fluid lost  
     by suction, 30  
   in shock, 154, 156  
   in sulfonamide therapy, 282,  
     290  
   in thyroid crisis, 743  
   in vomiting, 320  
   intramedullary admini-  
     stration of, 47  
   postoperative use of, 31, 32,  
     195, 612, 709, 746  
   preoperative use of, 110, 609,  
     647

Normal salt solution—Cont'd  
reactions following infusion  
of, 43

Nourishment, supplementary, in  
aged patient, 198

in burns, 545

in gastric surgery, 605

in hyperthyroidism, 730

in liver damage, 703

in malnutrition, 71, 107, 206

in thoracic surgery, 571, 584,  
590

in ulcerative colitis, 657, 658

Nupercaine, 435, 683

Nutrition, deficiencies of, in surgical  
patients, 106

principles of, 50

relation to healing of wound, 458,  
499

Nylon as dressing, 468, 530

## O

Obesity in surgical patient, 203

relation to postoperative wound  
infection, 497

to pulmonary embolism, 401

to venous thrombosis, 383

skin infections in, 346, 347

Obstipation as symptom of intestinal  
obstruction, 419

Obstruction, biliary (*see also* Biliary  
tract, jaundice):

as cause of persisting fistula,  
514

bronchial, in pulmonary atelec-  
tasis, 359, 360, 361, 368

in thoracic injury, 565

in wet lung, 566

intestinal, 415

as contraindication to barium  
meal, 642

caused by drains, 493

by peritonitis, 445, 450, 652

dehydration in, 417, 420

differential diagnosis of, 415,  
419, 421

enterostomy in, 644

etiology of, 415

following appendical perito-  
nitis, 445, 651, 652

surgery of colon, 672, 675

of small intestine, 643

high, 417

in gynecologic surgery, 785

in complete, use of Miller-  
Abbott tube in, 427

low, 417

mechanical, 415

diagnosis of, 419, 424, 426

Obstruction, intestinal mechanical  
—Cont'd

following use of drains, 493

gastric suction drainage in,  
426, 436

nonoperative treatment of,  
426, 436

operative treatment of, 421,  
437

postoperative care in, 439

preoperative preparation in,  
436

prophylaxis of, 424, 427

secondary to paralytic ob-  
struction, 441

oxygen therapy in, 436, 806

paralytic, 439

acute dilatation of stomach  
in, 453

associated with diffuse peri-  
tonitis, 440, 444, 450

with fractured pelvis, 441

with perforative appendi-  
citis, 447, 651, 652

with renal colic, 441

secondary to mechanical ob-  
struction, 423

strangulation in, 440

symptoms of, 440

treatment of, 440, 447

use of Miller-Abbott tube  
in, 427, 433

pathology of, 417

physical findings, in 419

postoperative, 415, 419, 424,  
624, 643, 669

use of Miller-Abbott tube in,  
427

strangulation in, 418, 420, 423,  
426, 436

suction drainage in, 426, 436

symptomatology of, 419

use of heat tent in, 435

x-ray evidence of, 421, 422

of colon, 665

pyloric (*see also* Congenital hyper-  
trophic pyloric stenosis):

gastric lavage in, 609

hypoproteinememia in, 707

in gastric disease, 600, 602, 609

postoperative, 632

preoperative care in, 608

vagus nerve resection in, 634

respiratory, after thyroidectomy,  
748

small intestine, causes of, 641

incomplete, 641

stomal, after gastroenterostomy,  
619

ureteral, postoperative, 793

- Obstructive resection of colon (*see* Colon)
- Occlusion of bronchus as cause of atelectasis, 359, 360, 361
- Occlusive arterial disease, 758 (*see also* Extremity)
- Ochsner treatment of diffuse appendical peritonitis, 447
- Ocular fundi, examination of, 250, 255
- Oenethyl, 100
- Oil, iodized (*see also* Lipiodol):  
in bronchography, 573, 584  
in cholangiography, 714  
in localization of lung abscess, 588
- Oliguria during sulfonamide therapy, 280, 286, 289, 291, 339  
in acute nephritis, 254  
in burns, 523, 524, 534  
in crushing injury, 140, 141  
in dehydration, 22, 26, 28  
in liver failure, 720  
in shock, 140  
in transfusion reaction, 182  
in uremia, 260  
treatment of, 261
- Omoxyoid muscle, 749
- Open drainage in empyema, 557
- Operating room, procedures in, 111
- Operation, abdominal, use of sulfadiazine in, 290  
of sulfanilamide in, 284, 647  
contraindicated in hemophilia, 219  
in shock, 110  
contraindications to, 107  
during pregnancy, 226  
effect of, on liver, 721  
emergency, preparation for, 110  
fluid replacement therapy during, 111  
for anal incontinence, 689  
for anorectal fistula, 687  
for bronchiectasis, 583  
for carcinoma of colon, 665  
of lung, 575, 581  
of stomach, 600, 608  
for congenital hypertrophic pyloric stenosis, 22, 194  
for intestinal obstruction, 437  
for lung abscess, 588, 589  
for parotitis, 412  
for pelvic abscess, 652  
for peptic ulcer hemorrhage, 629  
perforation, 631  
for peritonitis, 446, 650, 652  
for pruritus ani, 688
- Operation—Cont'd  
for pulmonary tuberculosis, 592, 595  
for subphrenic abscess, 406, 410  
in presence of anemia, 215  
notification of time of, 103  
on anus, 680  
on appendix, 646  
on biliary tract, 692  
on chest, 548  
on extremity, 756  
on small intestine, 641  
on stomach, 600  
optimum time for, in hyperthyroidism, 744  
permission for, 19, 103  
postponement of, 107, 143, 163, 192  
record of, 112  
relation of, to postoperative complications, 111  
to pulmonary atelectasis, 365  
embolism, 401
- Operative area, preparation of, 109  
technique, relation to healing of wound, 457
- Opium, 88  
alkaloids, 87  
use of, in ulcerative colitis, 657
- Oral sepsis as predisposing factor in parotitis, 411  
in surgical patient, 107, 202
- Orders, routine postoperative, 112  
preoperative, 108
- Organic disease (*see* Cardiac disease, Kidney disease, etc.)
- Orthostatic albuminuria, 256
- Oscillography, 762
- Osmotic balance, 23  
pressure of blood, 62  
relation to albumin, 62
- Osteomyelitis, chronic protein deficiency in, 64
- Otitis media, nephritis after, 254
- Ouabain, 246
- Oxidation in carbohydrate metabolism, 51, 52, 126  
in fat metabolism, 57, 126  
in protein metabolism, 61  
metabolic, role of vitamin B in, 208
- Oxygen, administration of, 804, 806  
by catheter, 809  
by inhaler, 811  
by mask, 809  
by positive pressure, in pulmonary edema, 805  
by tent, 806  
in anemia, 249  
in barbiturate overdose, 87

## Oxygen—Cont'd

- in burns, 537
  - in intestinal distention, 436, 806
  - in liver damage, 710
  - in morphine overdosage, 90
  - in paralytic intestinal obstruction, 441, 450
  - in paroxysmal dyspnea, 242
  - in postoperative pulmonary atelectasis, 368
  - in pulmonary embolism, 405
  - in shock, 155, 804
  - in test for viability of intestine, 438
  - in tetanus, 510
  - in thoracic surgery, 563, 566, 577, 594
  - in thyroid crisis, 743
  - surgery, 746
  - indications for use of, 804
  - liberation of, from hydrogen peroxide, 479
  - from zinc peroxide, 486
  - postoperative use of, 121, 610, 615, 631, 746, 751
  - requirement of, in anesthesia, 97, 98
  - saturation of blood, 24
  - supply, local, relation to wound healing, 457
  - transport, 24
  - with acornol penicillin, 585
- Oxygen-carrying capacity of blood, in anemia, 215
- Oxyhemoglobin, 24, 25

## P

- Pack in anorectal fistula, 687
  - in hemorrhoidectomy, 682, 683
  - in lung abscess, 588, 589
- Pain, after blood transfusion, 184
- after hemorrhoidectomy, 683, 684
  - after thyroidectomy, 745
  - as contributory cause of shock, 145
  - cardiac, 232
  - during cholangiography, 714
  - in biliary tract obstruction, 707, 714
  - in distention of urinary bladder, 330
  - in gangrene of extremity, 758, 763
  - in gas lacillus infection, 504, 505
  - in intestinal distention, 325
  - obstruction, 419, 421, 424, 641
  - in lung abscess, 376
  - in parathyroid tetany, 752
  - in parotitis, 411
  - in peptic ulcer, 600, 602, 605
  - relief of, by vagus nerve resection, 633
  - in peritonitis, 442, 443, 444

## Pain—Cont'd

- in postoperative hemorrhage, 495
  - in pulmonary atelectasis, 360
  - embolism, 384, 402, 403
  - in subphrenic space infection, 409
  - in thrombophlebitis, 384, 399
  - in wound disruption, 500
  - infection, 497
  - relief of, 87, 118
  - refrigeration for relief of, 769
- Pallor in anemia, 214
- in postoperative hemorrhage, 351
  - in pulmonary embolism, 402
  - in shock, 142
- Palmar spaces, infection of, 756, 757
- Pancreas in digestion of carbohydrates, 51
- of fat, 54
  - of protein, 60
  - hypotrophic effect of, 57
  - tissue extract in intermittent claudication, 767
- Pancreatic enzymes in duodenal fistula, 621
- Pancreatitis, chronic, as cause of fatty liver, 56
- in biliary duct obstruction, 716
- Pantopon, 92, 118
- Papain, use of, to prevent adhesions, 416
- Papaverine in nausea, 120
- in pulmonary embolism, 405
  - use of, with heparin, 389
- Para-aminobenzoic acid as sulfonamide inhibitor, 277
- Parachlorophenol in treatment of infected wounds, 483
- Paradoxical respiration, 594
- Paraldehyde, 84, 240
- Paralysis, inferior laryngeal nerve, 748
- phrenic nerve, 343, 597
- Paralytic intestinal obstruction (see Obstruction, intestinal, paralytic)
- Parasitic infection, anemia in, 214
- intestinal, as diagnostic problem, 105
- Parasympathetic depressant drugs, preoperative use of, 93, 94
- nerve supply of bladder, injury to, 676
  - stimulants in paroxysmal tachycardia, 234
  - in urinary retention, 331
- Parathyroid deficiency, 751
- glands, removal of, 751
  - hormone, 752, 753
  - tetany, 751 (see also Tetany, parathyroid)

Paregoric as sedative, 90, 119, 196  
 in anal incontinence, 687  
 plastic operation, 689  
 in burns of perineum, 531  
 in colostomy diarrhea, 679  
 in ulcerative colitis, 658  
 Parenteral fluid therapy (*see* Fluid replacement therapy, Infusion, Dextrose, Normal salt solution, etc.)  
 Paresis of intestine, postoperative, 324, 415, 417, 421  
 Parotitis, postoperative, 470  
 Paroxysmal dyspnea, 241  
 tachycardia, 234  
 Passive vascular exercise, 766  
 Patient, responsibility of surgeon to, 19  
 Pavex apparatus, 766  
 Pectin in treatment of shock, 153, 156  
 effect of, on liver function, 153  
 Pediatrician, cooperation with, 191  
 Pellagra, 210  
 Pelvic abscess (*see* Abscess, pelvic)  
 Inflammatory disease, operation for, 780  
 operation, complications following, 789  
 Pelvis, fractured, intestinal atony with, 441  
 Penicillin, 297  
 administration of, 300, 302  
 aerosol, 585, 590  
 chemical structure of, 298  
 delayed absorption of, 301  
 dermatitis caused by, 300  
 discovery of, 276  
 dosage of, 300, 301  
 excretion of, 298, 300  
 fastness, 299  
 forms of, 297  
 indications for use of, 301, 303  
 inhibitors, 299, 302  
 international standard of, 299  
 local injection of, 303, 305  
 use of, as wound irrigation, 677  
 in gangrene, 768  
 in thoracic cavity, 582  
 mode of action of, 298  
 oily suspension of, 302  
 organisms resistant to, 299  
 procaine combination, 302  
 production of, 297  
 resistance to, 299  
 salts of, 298  
 sensitization to, 298, 300  
 source of, 297  
 toxic effects of, 300  
 treatment of, 301

Penicillin—Cont'd  
 unit of activity of, 299  
 use of, in agranulocytosis, 280, 305, 734  
 in appendical abscess, 651  
 in arthritis, 301  
 in bronchitis, 319  
 in bronchopneumonia, 373, 374  
 in burns, 537, 539, 544  
 in carbuncle, 301, 305, 347  
 in cellulitis, 486, 756  
 in colon surgery, 668, 675  
 in decubitus ulcer, 346  
 in duodenal fistula, 622  
 in empyema, 300, 301, 559  
 in furunculosis, 301, 305, 346  
 in gas gangrene, 506, 507  
 in gastric surgery, 608, 616  
 in hemothorax, 569  
 in infected gangrene, 769  
 in intestinal obstruction, 437  
 in oral sepsis, 203  
 in parotitis, 412  
 in peptic ulcer hemorrhage, 630  
 perforation, 630, 631  
 in peritonitis, 300, 313, 448, 651  
 in pulmonary atelectasis, 372  
 in septicemia, 357  
 in skin-grafting, 542  
 in tetanus, 511  
 in thoracic surgery, 301, 562, 563, 565, 579, 591  
 in ulcerative colitis, 657  
 in urinary tract infection, 340  
 in wound dehiscence, 502  
 infection, 301, 481, 483, 675  
 Penicillinase, 299, 302, 448, 481  
*Penicillium notatum*, 276, 297  
 Penrose drains, 492  
 Pentnucleotides in agranulocytosis, 280, 734  
 Pentothal (*see* Sodium pentothal)  
 Pepsin in gastric juice, 603  
 in protein digestion, 60  
 Peptic ulcer (*see* Stomach, ulcer of, Duodenum, ulcer of)  
 Peptidases, 61  
 Peptide linkage, 59  
 Peptides in protein digestion, 60  
 hydrolysate, 70  
 Peptone hydrolysate, 206  
 Peptones in protein digestion, 60, 603  
 Percussion in acute gastric dilatation, 451  
 in intra-abdominal hemorrhage, 351  
 in urinary retention, 330  
 Perforation in acute appendicitis, 443, 649, 652

Perforation in acute appendicitis  
—Cont'd

- conservative treatment, 447, 650, 652
- operative treatment, 649, 650, 651, 652
- of gastrointestinal tract, as cause of peritonitis, 442, 443
- of ileum, 444
- of peptic ulcer, 630, 634
- of stomach, 444, 632
- of viscus, caused by drains, 492
- Perianal infection, 689
- Perineal resection (*see* Rectum, perineal resection of)
- wound, care of, 676
- Perineum, burns of, 531
- surgery of, postoperative care in, 783, 788, 789
- Peripheral circulatory failure (*see* Shock)
- vascular bed, disturbance of, in shock, 132, 138
- disease 738 (*see also* Extremity, occlusive arterial disease of)
- Perirectal abscess, 689
- Peristalsis, intestinal, in acute gastric dilatation, 451
- in enterostomy, 644, 646
- in mechanical intestinal obstruction, 418, 419, 642
- in paralytic intestinal obstruction, 439, 441
- in parathyroid tetany, 752
- in peritonitis, 444, 446, 449
- in protein deficiency, 67
- postoperative detection of, 425, 449
- return of, 126, 325, 326, 415, 631, 651
- reverse, 432
- stimulation of, by drugs, 326, 327, 328, 441, 450
- by enemas, 326, 441, 450
- by heat tent, 117, 326, 441, 450
- by stipes, 326, 441, 450
- contraindicated in mechanical obstruction, 424
- in surgery of colon, 669
- Peristaltin, 326
- Peritoneal abscess, 443, 446, 492, 493, 631, 649, 650, 651, 652
- adhesions, postoperative, 416, 417, 641, 652, 653
- cavity, drainage of, 493, 648, 649
- hemorrhage into, 351
- exudate in intestinal obstruction, 438

Peritoneal exudate—Cont'd

- in peritonitis, 442, 444, 445, 446, 648, 649, 653, 654
- postoperative, 416
- fluid, culture of, 647
- Peritonitis, 415, 442
- acute gastric dilatation in, 451, 453
- adhesions in, 417, 442, 445, 648, 651, 652
- antecedent to mechanical intestinal obstruction, 442, 445, 450, 652
- to paralytic intestinal obstruction, 440, 445, 450, 652
- to pelvic abscess, 446, 651
- to subphrenic abscess, 406, 409, 445, 651
- aseptic, 442
- biliary, 720
- chemical, 442
- diagnosis of, 442, 443, 444
- diffuse, 443, 652
- causative bacteria in, 444
- etiology of, 442
- following appendicitis, 448, 652
- colon surgery, 663, 669
- colostomy, 672, 675
- enterostomy, 439
- gastric surgery, 615, 624
- peptic ulcer perforation, 632
- surgery of small intestine, 643
- Towler position in, 115
- generalized, 649
- enterostomy in, 644
- hiccup in, 342
- infective, 442
- intestinal obstruction following, 440, 445, 450, 652
- localized, 442, 445
- in perforative appendicitis, 648, 649, 650
- paralytic intestinal obstruction in, 440, 450
- penicillin therapy in, 298, 300, 313, 448, 651
- routes of spread, 445
- septicemia with, 355
- spreading, 443, 648
- treatment of, 446, 653
- with penicillin, 298, 300, 303, 313, 448, 651
- with streptomycin, 309, 313, 448
- with sulfadiazine, 448, 651
- Permission for operation, 19, 103
- Pernicious anemia, 217
- Pernoston, 85
- Perspiration, loss of fluid by, 22, 122

Petechial hemorrhages in purpura, 225  
 in scurvy, 218  
 in urinary bladder mucosa, 330  
 Petrolatum-impregnated gauze, 468, 527, 528  
 pH of blood, 25  
 Phenodorn, 85  
 Pharyngitis, as contraindication to operation, 107, 192, 364  
 postoperative, 317  
 Phenobarbital, as hypnotic, 85  
 as sedative, 83, 86  
 in angina pectoris, 248  
 in hyperthyroidism, 729  
 in tetanus, 511  
 sodium (*see* Sodium phenobarbital)  
 Phenosulfonphthalein, excretion test, 257  
 in diagnosis of fistula, 513  
 Phenylalanine, 59  
 Phlebitis (*see* Thrombophlebitis)  
 Phlebography in diagnosis of venous thrombosis, 385  
 Phlebothrombosis (*see* Thrombosis, venous)  
 Phlegmasia alba dolens, 380, 381, 398  
 Phosphatase, acid, serum, 799  
 alkaline, serum, 602, 697, 799  
 Phospholipids, 55, 56  
 Phosphoric acid, 25  
 Phosphorus, inorganic, serum, 799  
 in hypoparathyroidism, 752  
 in vitamin D deficiency, 212  
 Photography, clinical, 105  
 Phrenic nerve, interruption of, in hiccough, 343  
 after surgery for tuberculosis, 597  
 Phthalylsulfathiazole (*see* Sulfathalidine)  
 Physical examination, 104  
 in aged patient, 197  
 in children, 191  
 in obese patient, 203  
 preoperative, 102  
 findings in acute gastric dilatation, 451  
 in appendical abscess, 650  
 in arteriovenous fistula, 774  
 in bronchopneumonia, 372  
 in cystitis, 337  
 in diffuse peritonitis, 444  
 in functional cardiac disorders, 231  
 in gas bacillus infection, 504  
 in hyperthyroidism, 728, 743

Physical examination—Cont'd  
 in intestinal obstruction, mechanical, 419  
 paralytic, 440  
 in localized peritonitis, 442  
 in lung abscess, 375  
 in occlusive arterial disease, 758  
 in parathyroid tetany, 752  
 in parotitis, 410  
 in pelvic abscess, 651  
 in postoperative hemorrhage, 351  
 in pulmonary atelectasis, 360  
 embolism, 401  
 in shock, 142  
 in subphrenic space infection, 409  
 in tetanus, 409  
 in thyrocardiac disease, 740  
 in venous thrombosis, 383  
 in wound dehiscence, 500  
 infection, 497  
 Physiologic regulation of fluid and electrolyte balance, 22  
 Physiology, contributions to surgery, 50, 69, 102  
 Physostigmine, 326  
 Picrotoxin, 87  
 Pitkin's menstruum, 389, 391  
 Pitressin as peristaltic stimulant, 326  
 Pituitary gland, relation of, to thyroid gland, 725, 726, 732  
 thyrotropic hormone of (*see* Thyrotropic hormone)  
 Pituitrin as peristaltic stimulant, 326, 803  
 Placebo, use of, in hypodermic injections, 88  
 Placental blood, use of, for transfusion, 185  
 Plasma (*see also* Albumin, Blood, Globulin, Hypoproteinemia, etc.):  
 albumin, 62  
 concentrated, for transfusion, 150, 151  
 concentration of, in plasma, 62  
 functions of, 62, 65, 151  
 globulin ratio, 62, 65  
 loss of, in albuminuria, 256  
 in starvation, 65  
 origin of, 62  
 osmotic effects of, 62, 151  
 bank, 150, 820, 828  
 bicarbonate, 25  
 carbonic acid, 25  
 chloride, 28, 31, 32, 33, 798  
 chlorides, in burns, 523, 538  
 restoration of, 31, 32

## Plasma—Cont'd

- fibrinogen, 62
  - elevation of, after operation, 382
- globulin, 62
  - concentration of, 62
  - elevation of, postoperative, 382
  - functions of, 62, 63
  - in hemophilia, 219
  - specificity of, 58
  - synthesis of, 62
- ionic concentration of, 23
- loss of, in burns, 522, 523, 532
  - in intestinal obstruction, 418, 437
  - in shock, 135, 136, 137, 138, 141, 149
- preserved, 150
  - storage of (Baxter), 820
  - storage of (Cutter), 828
- proportion of, in body weight, 21
- proteins, 62
  - concentration of, 62, 69
  - deficiency of, 34, 63, 64, 65, 79
    - relation to tissue protein loss, 63, 64, 69, 79
  - functions of, 62, 63
  - in cephalin-cholesterol flocculation test, 701
  - in dehydration, 28, 63, 65, 66
  - in malnutrition, 28, 64, 65
  - osmotic pressure of, 151
  - postoperative changes in, 382
  - regeneration of, 63, 64, 79
- specific gravity of, 162
- transfusion, 148
  - cross-matching unnecessary in, 68, 151
  - in burns, 68, 525, 533, 534
  - in shock, 137, 139, 147, 156, 159, 162
  - intramedullary, 46
  - limitations of, 147
  - nomogram for determination of dosage, 148
  - reactions following, 151
  - unit, of, 150
  - volume, variations in, 65, 66
  - water, percentage of body weight as, 21
- Plaster dressing for burns, 530
- Platelets, blood, in hemophilia, 219
  - in thrombocytopenic purpura, 224, 225
    - postoperative elevation of, 382
- Pleural cavity, apparatus for suction drainage of, 554, 555, 556
  - aspiration of, in chest wound, 564, 565
    - in differential diagnosis, 574

## Pleural cavity aspiration—Cont'd

- in empyema, 553
- in hemothorax, 568, 569
- in tension pneumothorax, 567
- postoperative, 566, 580
- drainage of, by intercostal catheter, 553, 555, 562
- in thoracic surgery, 562
- infection of (*see also* Empyema):
  - in diagnostic aspiration, 372, 410, 574
  - in lung abscess, 587, 589, 590
  - in subphrenic abscess, 409
- Pleurisy as cause of hiccough, 342
- Pneumectomy, mortality rate of, 581
  - postoperative care in, 580
  - complications of, 580, 581
  - thoracic alterations after, 579
- Pneumonia (*see also* Bronchopneumonia, pulmonary respiratory):
  - after biliary tract surgery, 710, 717
  - after gastric surgery, 615, 618
  - after pneumectomy, 581
  - after pulmonary atelectasis, 372
  - after subphrenic abscess, 409
  - after thyroidectomy, 751
  - after tracheobronchitis, 319, 349
  - as complication of lung abscess, 587, 591
  - aspiration, 374
  - bronchial, 372
  - differentiation of, from pulmonary embolism, 403, 404
  - empyema following, 550
  - in aged patient, 200
  - in burns, 524, 525, 537
  - influenzal, 550
  - pneumococcal, 550
  - postoperative, 632
    - relation of protein deficiency to, 67
  - streptococcal, 550
  - treatment of, with oxygen, 804
    - with penicillin, 297, 303
    - with streptomycin, 314
    - with sulfonamide drugs, 287, 288, 290, 292
  - unresolved, 551
  - virus type, serum agglutinins in, 163
- Pneumoperitoneum, postoperative, 115, 116
- Pneumothorax, artificial, as diagnostic procedure, 573
  - contraindications to, 574, 586
  - in lung abscess, 586
  - complicating empyema, 552



Pneumothorax—Cont'd  
 effects of, on respiration, 548  
 following thoracic surgery, 563, 580  
 tension, 549  
   after chest wound, 564  
   treatment of, 567  
 Pneumotomy for drainage of lung  
   abscess, 587, 588  
 Pocketing in empyema, 551, 552, 560, 561  
 Polya operation, 624  
 Polypeptides, 59, 60  
 Polyuria, 257  
 Polyvalent serum, use of, in gas  
   bacillus infection, 505, 506  
 Pontocaine for anesthetization of  
   nasopharynx, 430  
 Popliteal vein, compression of, in  
   Fowler position, 115, 381  
 Portal vein, obstruction of, 351  
 Position after anoplastic surgery,  
   690  
   after drainage of empyema, 553, 558  
   after thyroidectomy, 744  
   for bronchoscopy, 371  
   for gastric lavage, 321  
   for paroxysmal dyspnea, 242  
   tachycardia, 234  
   for postural drainage, 575  
   for proctoscopy, 680  
   for prophylaxis of decubitus ulcer,  
     115, 344  
   for relief of urinary retention, 329,  
     331, 332  
   for sigmoidoscopy, 680  
   for tracheobronchial suction, 369,  
     371  
   Fowler, 114, 447 (*see also* Fowler  
     position)  
   in acute gastric dilatation, 453  
   in congestive cardiac failure, 239,  
     240  
   in diffuse peritonitis, 447  
   in pulmonary atelectasis, 365, 367,  
     368  
   in shock, 145, 156  
   in thrombophlebitis, 398  
   in venous thrombosis, 381, 381,  
     385  
   postoperative, 114, 116  
     change of, 116, 367, 385, 594,  
       692, 710  
     during anesthetic recovery, 112  
     in gastric surgery, 610, 617  
     in thoracic surgery, 577  
     relation to pulmonary atelec-  
       tasis, 365

Position—Cont'd  
 Trendelenburg, after total gas-  
   trectomy, 615  
   in postural drainage, 575  
 Positive nitrogen balance, 62  
 Postanesthetic vomiting, 113, 120,  
   320  
 Postoperative acidosis, 123, 126, 320  
   albuminuria, 254  
   ambulation, delayed, 128  
     early, 129  
   bronchitis, 318, 349, 359  
   bronchopneumonia, 372  
   carbuncle, 346  
   care, aims of, 18  
     general measures, 111  
     in aged patient, 199  
     in amputation of extremity, 772  
     in anorectal surgery, 682, 687,  
       689  
     in appendicitis, 646, 648  
       perforative, 651  
     in arteriovenous fistula, 777  
     in biliary tract surgery, 709  
     in cardiac disease, 239  
     in cholecystectomy, 710  
     in cholecystostomy, 711  
     in choledochostomy, 711  
     in colon surgery, 668  
     in colostomy, 666, 670, 678  
     in congenital hypertrophic pyloric  
       stenosis, 195  
     in diabetes, 271  
     in gastric surgery, 610, 615  
     in gynecologic surgery, 784  
     in infants and children, 195  
     in infections of extremity, 493,  
       756, 757, 764  
     in intestinal obstruction, 439  
     in obese patient, 204  
     in peptic ulcer perforation, 631  
     in perineal surgery, 789  
     in small bowel surgery, 612  
     in thoracic surgery, 562, 566,  
       577  
       after lobectomy, 581  
       after pneumonectomy, 577,  
       579  
       after thoracoplasty, 594  
       for bronchiectasis, 586  
       for lung abscess, 588, 590  
       for tuberculosis, 593, 591,  
       597  
     in thyroid surgery, 745  
     in ulcerative colitis, 658  
     in vagus nerve resection, 635  
     in vesicovaginal fistula, 794  
 Miller-Abbott tube in, 427  
 of skin, 343  
 value of encouragement in, 131

Postoperative—Cont'd  
 catheterization, routine, 333  
 complications in hypertensive patients, 252  
   in nephritic patient, 255  
   in obese patient, 204  
   in thyrocardiac disease, 742  
   major, 349  
   minor, 317  
   of abdominoperineal resection, 675  
   of biliary tract surgery, 717  
   of colon surgery, 669  
   of colostomy, 672  
   of gastric surgery, 647  
     after total gastrectomy, 615  
   of gynecologic surgery, 785, 789  
   of hemorrhoidectomy, 683  
   of small bowel surgery, 643  
   of thoracic surgery, 563  
     after lobectomy, 582  
     after pneumonectomy, 580  
     in lung abscess, 589, 591  
   of thyroidectomy, 747  
 prevention of, 120  
   in aged patient, 199  
   psychologic factors in, 104  
 pulmonary, 358 (see also Atelectasis, pulmonary, Pneumonia, Lung abscess, Pulmonary complications, post-operative, etc.)  
   relation of sedation to, 92  
   relation of protein deficiency to, 67  
   to operation, 111  
   to wound healing, 457, 499, 500  
 conjunctivitis, 317  
 cyanosis, 113, 122, 204, 360, 577  
 decubitus ulcer, 343  
 dehydration, 123, 320 (see also Dehydration)  
 depression of kidney function, 31  
 diet (see Diet)  
 elimination, 126  
 examination, 19  
 febrile state (see Fever)  
 fluid balance, maintenance of, 122  
   replacement therapy (see Fluid replacement therapy)  
 furunculosis, 346  
 gangrene of skin, 343  
 gas pains, 325  
 gastric dilatation, 451, 618, 634  
   retention, 610, 611, 634, 636  
 hemoclastic crisis, 705  
 hemorrhage, 350, 495  
   in hypertensive patients, 252

Postoperative hemorrhage—Cont'd  
   in jaundice (see Bleeding tendency, jaundice)  
   in thoracic surgery, 563  
   incisional, 495  
   treatment of, 352  
 hiccough, 342  
 infection (see special headings)  
 insomnia, 119  
 intestinal distention, 324  
   obstruction (see Obstruction, intestinal)  
 lung abscess, 375  
 nausea, 120, 125, 320  
 orders, routine, 112  
 parotitis, 410  
 paroxysmal tachycardia, 234  
 peritonitis, 443 (see also Peritonitis)  
 pharyngitis, 317  
 pneumonia (see Pneumonia, Bronchopneumonia, etc.)  
 position, 114 (see also Position)  
 prothrombin deficiency, 224, 707, 717  
 pulmonary atelectasis, 359 (see also Atelectasis, pulmonary)  
   embolism, 400 (see also Embolism, pulmonary)  
   rehabilitation, 19  
   restriction of sodium chloride, 32  
 salt intolerance, 32  
 sedation, 118  
 shock, 66, 139, 349, 581, 617, 710  
   in children, 193  
 stupor, due to oversedation, 93  
 subphrenic space infection, 409  
 tracheitis, 349, 748  
 uremia, 260  
 urinary incontinence, 330, 787  
   output, 330  
   retention, 328, 676, 787  
   tract infection, 337  
 venous thrombosis, 377  
 vomiting, 113, 120, 123, 320  
 weight loss, 64  
 wound dehiscence, 499  
   infection, 496  
 Postural drainage, 575, 584, 586  
 exercises, 766  
   treatment of pulmonary atelectasis, 368  
 Potassium ion, in body fluids, 23  
   shift of, in stored blood, 187  
   loss of, in infantile diarrhea, 33  
   permanganate as vaginal douche, 782  
   as wound irrigation, 677  
   use of, in fluid replacement therapy, 34

- Preanesthetic medication, 92, 99  
 Pregnancy, fatty liver in, 56, 57  
   surgery during, 226  
 Premature contraction, cardiac, 232  
   labor, 226, 227  
 Preoperative care, aims of, 17  
   blood transfusion in, 106, 162  
   complicating factors in, 190  
   correction of malnutrition in, 205  
   in abdominoperineal resection, 675  
   in aged patients, 197, 198  
   in amputation of extremity, 768  
   in anal plastic operation, 689  
   surgery, 681  
   in anemic patient, 215  
   in angina pectoris, 248  
   in appendical abscess, 650  
   in appendicitis, 646, 647  
   in arteriovenous fistula, 774  
   in biliary tract surgery, 692  
   in bronchiectasis, 584  
   in cardiac disease, 232, 238  
   in children, 190, 192  
   in colon surgery, 661  
   in congenital hypertrophic pyloric stenosis, 194  
   in congestive cardiac failure, 238, 239  
   in diabetes, 262, 265  
   in emergency operation, 110  
   in gastric surgery, 602, 604, 606, 609  
   in gynecologic surgery, 779  
   in hemolytic jaundice, 216, 705  
   in hemophilia, 219  
   in hypertension, 250, 252  
   in hyperthyroidism, 728  
   in hypoproteinemia, 106  
   in infants, 190  
   in intestinal obstruction, 426, 436  
   in jaundice, 695, 704, 708  
   in lung abscess, 586  
   in marginal ulcer, 626  
   in metabolic disorders, 106  
   in nephritis, 255, 259  
   in nutritional deficiency, 68, 106  
   in obese patient, 203  
   in occlusive arterial disease, 763, 765  
   in prothrombin deficiency, 220, 224, 705  
   in purpura, 225  
   in pyloric obstruction, 608  
   in rectovaginal fistula, 783  
   in small intestinal surgery, 642  
   in thoracic surgery, 570, 590  
 Preoperative care in thoracic surgery  
   —Cont'd  
     for lung abscess, 590  
     for tuberculosis, 596  
     in thoracoplasty, 593  
     in ulcerative colitis, 657  
     in vagus nerve resection, 635  
     in vesicovaginal fistula, 794  
     indications for use of Miller-Abbott tube in, 427, 436  
     psychologic factors in, 103, 191,  
       tests for prothrombin deficiency,  
       in, 220  
   catheterization, 109  
   dehydration, correction of, 106  
   enema, 109  
   examination, 17, 102, 104  
   gastric suction, prophylactic, 325  
   infection, foci of, 107  
   laboratory tests, 104, 105  
   medication, 83, 92, 108, 783  
     before local anesthesia, 95  
     in cardiac patient, 238, 239  
     in children, 93, 191  
     in hypertension, 251  
     relation to pulmonary atelec-  
       tasis, 364  
   orders, 108  
   vitamin deficiency, correction of,  
     107  
   x-ray of chest, 105  
     in children, 192  
     in lung disease, 358  
 Pressure dressing for wound, indica-  
   tions for, 465  
   technique of application, 465  
   in burns, 526  
 Primary anemia, 213  
   shock, 133, 144, 155  
 Priodax, 803  
 Probing of fistula, 513  
 Procaine in determination of via-  
   bility of intestine, 438  
   in intercostal block in thoracic  
   surgery, 565, 578  
   in regional sympathetic ganglion  
   block, 763, 767  
   in venipuncture, 178  
 Procaine-penicillin, 302  
 Proctocaine, 684  
 Proctoclysis, 35  
 Proctoscopy, 680  
 Progesterone for prevention of  
   abortion, 227  
 Prognosis (see Surgical risk)  
 Proline, 59  
 Prophylaxis of bleeding tendency  
   in jaundice, 224, 706  
   of decubitus ulcer, 115, 116, 344  
   of gas bacillus infection, 505

## Prophylaxis—Cont'd

- of intestinal obstruction, 325, 424
- of major postoperative complications, 349
- of minor postoperative complications, 317
- of parotitis, 411
- of postoperative complications, 120
  - in aged patient, 199
- of pulmonary complications, 199, 364, 404
- of respiratory tract infection, 358
- of shock, 143, 162, 349
- of tetanus, 508
- of urinary retention, 329
  - tract infection, 337
- of venous thrombosis, 385
- of wound infection, 497
- Propylthiouracil, 736, 741
  - dosage of, 737
  - in prevention of thyroid crisis, 742, 744, 747
  - precautions during use of, 737
  - toxic effects of, 736
  - use of iodine with, 736, 737
- Prostate, hypertrophy of, as cause of urinary retention, 329, 337, 676
- Prostigmin in intestinal distention, 327, 441
  - in prophylaxis of venous thrombosis, 387
  - in urinary retention, 327, 331
- Protamine in heparin overdosage, 392
  - sulfate in purpura, 225
  - zinc insulin, 264, 272
- Protein as source of energy, 60
- deficiency (*see also* Hypoproteinemia)
  - acute, 64, 68
  - associated with anemia, 67, 162, 214
    - with vitamin deficiency, 67, 79, 209
  - chronic, 64, 68, 78, 79, 106, 205
  - effects of, 66, 79, 205
  - estimation of, 64, 69
  - in aged patient, 198, 201
  - in burns, 64, 523, 545
  - in cachectic disease, 64, 205
  - in empyema, 64, 560
  - in enterostomy, 645
  - in hemorrhage, 64, 68
  - in hypermetabolism, 64, 730
  - in intestinal obstruction, 64, 419
  - in nephritis, 259
  - in osteomyelitis, 64
  - in shock, 64, 68
  - in trauma, 64, 68

## Protein deficiency—Cont'd

- in ulcerative colitis, 657
- postoperative, 64
- reduced blood volume in, 69
- relation to hypoproteinemia, 63, 79
- treatment of, 65, 68, 70, 76, 78, 106, 206 (*see also* Protein replacement therapy)
  - by blood transfusion, 68, 69, 78, 107, 162
  - by plasma transfusion, 68, 69, 78, 107, 163
- dietary, 60, 62
  - daily requirement of, 60, 79
  - relation to wound healing, 130, 458, 499, 500
- digestion, 60, 603
- equilibrium, 61, 63
- hydrolylate, administration of,
  - by infusion, 74, 76, 77
  - reactions to, 76
  - by mouth, 72
  - by tube, 73, 74, 615
- in jejunostomy feeding, 615
- in paralytic intestinal obstruction, 441
- in peptic ulcer, 67, 606
- postoperative use of, 125, 616, 631, 668, 709, 788
- preoperative use of, 107, 571, 607
- labile reserve of, 61
- metabolism, 55, 58, 61
  - nitrogen balance in, 62
  - role of liver in, 61, 693
- plasma, 62, 800 (*see also* Plasma proteins)
- replacement therapy, 68, 74, 78 (*see also* Protein deficiency, treatment of)
  - in anemia, 216
  - in burns, 68, 546
  - in chronic protein deficiency, 68, 76, 107
  - in empyema, 560
  - in enterostomy patient, 645
  - in gastric surgery, 605, 606, 609, 612, 614, 626
  - in gastrointestinal tract disease, 72
  - in hemorrhage, 68
  - in hyperthyroidism, 730, 731
  - in liver damage, 56, 703
  - in malnutrition, 107, 206
  - in nephritis, 259, 260
  - in peritonitis, 449
  - in septicemia, 355
  - in shock, 68, 148
  - in sternal block, 619

- Protein replacement therapy—Cont'd  
 in ulcerative colitis, 657  
 milk protein concentrates in, 72  
 oral, 70  
 sipper apparatus, in, 73  
 skin milk powder in (*see also* Skim milk), 72  
 reserve, 61  
 sensitivity, 58, 509  
 sparing effect of carbohydrate, 52, 78, 126  
 specific dynamic action of, 730  
 structure of, 59  
 substitutes, 69  
*Proteus vulgaris* as contaminant of wound, 466, 475  
 effect of streptomycin on, 313  
 of sulfadiazine on, 290  
 of sulfasuxidine on, 294  
 of tyrothricin on, 484  
 in burn infections, 538, 544  
 in flora of skin, 477  
 in urinary tract infection, 340  
 in wound infection, 483, 486, 487  
 Prothrombin, concentration of, 220, 706  
 relation to hemorrhagic tendency, 219, 706  
 deficiency of, 220, 571, 705, 707  
 causes of, 220, 705, 707  
 in absence of jaundice, 707  
 in jaundice, 219, 226, 705  
 in liver damage, 707  
 tests for, 220  
 treatment of, 706  
 determination of, quantitative, 220  
 in bank blood, 187  
 in blood-clotting mechanism, 163, 219  
 postoperative decrease of, 224, 706  
 restoration of, by blood transfusion, 164, 352, 707  
 synthesis of, 212, 694, 707  
 as test of liver function, 701  
 effect of protein deficiency on, 67  
 time determination, 221, 705  
 Pruritus ani, treatment of, 688  
*Pseudomonas aeruginosa* as contaminant of wound, 466, 475  
 effect of penicillin on, 299  
 of streptomycin on, 313  
 of sulfonamide on, 287, 290  
 of tyrothricin in, 484  
 in burn infections, 538, 544  
 in flora of skin, 477

- Pseudomonas aeruginosa*—Cont'd  
 in urinary tract infection, 340  
 in wound infection, 483, 486, 487  
 Psychiatrist as aid in gynecology, 779  
 Psychic disturbance in aged patient, 201  
 in children, 191  
 in hyperthyroidism, 726, 728, 742  
 in shock, 133, 134, 139  
 Psychologic factors in convalescence, 131  
 in postoperative complications, 104  
 in preoperative care, 83, 103  
 Psychoneurosis associated with cardiac symptoms, 231  
 Ptyalin in carbohydrate digestion, 50  
 Pulmonary atelectasis, 359 (*see also* Atelectasis, pulmonary)  
 complications, postoperative, 107, 108, 358, 750  
 causes of, 359  
 due to oral sepsis, 107, 202, 364  
 following oversedation, 118, 364  
 in cardiac subjects, 239  
 in gastric surgery, 618  
 in gynecology, 790  
 in thoracic surgery, 563, 580, 581, 582, 590  
 oxygen therapy in, 805  
 prevention of, 121, 199  
 congestion in cardiac disease, 239, 240  
 decortication (*see* Decortication, pulmonary)  
 disease, anesthesia in, 97, 98, 99  
 use of oxygen in, 805  
 edema (*see* Edema, pulmonary)  
 embolism (*see* Embolism, pulmonary)  
 gangrene, 374, 475, 586  
 infarction, 402  
 regulation of acid-base balance, 27  
 tuberculosis, 591  
 Pulse rate, effect of digitalis on, 238, 244  
 in acute gastric dilatation, 451, 619  
 in auricular fibrillation, 326, flutter, 235  
 in bronchopneumonia, 372  
 in cardiac failure, 244  
 in diffuse peritonitis, 443  
 in emotional conflict, 233  
 in gas gangrene, 504

- Pulse rate—Cont'd  
 in hemorrhage, 350, 495  
 in hyperthyroidism, 233, 727, 729, 738, 745  
 in infection, 233  
 in intestinal obstruction, 420, 421  
 in paralytic intestinal obstruction, 440  
 in paroxysmal tachycardia, 234  
 in pulmonary atelectasis, 360  
 embolism, 402  
 tuberculosis, 233  
 in septicemia, 354  
 in shock, 142, 350  
 in sinus arrhythmia, 233  
 in thyrocardiac disease, 740, 742  
 in thyroid crisis, 742, 743  
 in venous thrombosis, 384  
 in wound dehiscence, 500
- Pump, suction, for ileostomy, 659
- Purpura, allergic, 224  
 hemorrhagic, 224  
 thrombocytopenic, 164, 224  
 toxic, 224
- Pus as sulfonamide inhibitor, 277
- Pyelitis, postoperative, 337, 793
- Pylephlebitis, suppurative, in appendicitis, 652
- Pylorus, obstruction of, 66, 603 (*see also* Congenital hypertrophic pyloric stenosis)
- Pyrikenzamine, 185, 301, 688
- Pyridium, 341
- Pyridoxine, 210, 734
- Pyrogens, 43
- Pyrogenic reaction following blood transfusion, 184  
 infusion, 43  
 prevention of, 43, 184
- Pyruvic acid in carbohydrate metabolism, 52  
 in removal of burnt slough, 487, 543
- Pyuria, 338

## Q

- Quick test, for prothrombin deficiency, 221  
 of liver function, 699, 702
- Quinidine, use of, in auricular fibrillation, 237  
 flutter, 235  
 in paroxysmal tachycardia, 234  
 in premature contraction, 233  
 in thyrocardiac disease, 741

## R

- Radiation sickness, 210
- Radioactive iodine, 739

- Radium application in postoperative parotitis, 411
- Ratio, albumin-globulin, 62, 65
- Carbonic acid-bicarbonate, 25
- Rayon as dressing, 469, 530
- Reaction, hemolytic, 183  
 protein sensitivity, 58, 509  
 pyrogenic, 43, 184  
 to infusion of crystalloids, 43  
 of gelatin, 153  
 of protein hydrolysate, 76  
 to transfusion of blood, 140, 165, 179, 181  
 caused by cold agglutinins, 168  
 by Rh incompatibility, 170  
 of bovine serum albumin, 153  
 of plasma, 151  
 of serum albumin, 152
- Reassurance, 103
- Rectal bleeding as symptom of carcinoma of colon, 661  
 examination in pelvic abscess, 651  
 tube in intestinal distention, 326, 441, 450  
 postoperative use of, 127, 785
- Rectum, abdominoperineal resection of, 675  
 postoperative complications in, 675  
 preoperative care in, 675  
 carcinoma of, diagnosis of, 680  
 perineal resection of, 677  
 surgery of, urologic complications in, 675
- Red blood cells (*see also* Erythrocytes)  
 in treatment of wounds, 489, 768
- Reflex inhibition as cause of acute gastric dilatation, 452  
 spasm in pulmonary embolism, 403  
 in thrombophlebitis, 400
- Refrigeration of extremity, 769  
 technique of, 770
- Regulation of acid-base balance by kidneys, 26  
 by lungs, 24  
 of body heat by fluid loss, 22, 122  
 of fluid and electrolyte balance, 21
- Regurgitation in acute dilatation of stomach, 452  
 in diffuse peritonitis, 444  
 in intestinal obstruction, 417, 432
- Rehabilitation, postoperative, 19
- Removal of drains, 494, 757  
 of sutures, 463, 747
- Renal (*see* Kidney)

Repair of divided recurrent laryngeal nerve, 749

Reperitonization, 416

Resection of colon, 668

  of lung, 576, 580, 583, 589, 595

  of rectum, 675, 677

  of stomach, 600, 608, 624, 630, 635

Residual urine, relation to urinary tract infection, 337

Respiration, paradoxical, 597

  physiology of, 548

  relation to venous thrombosis, 381

Respiratory depression in barbiturate overdosage, 86

  in morphine overdosage, 89

  difficulty, Fowler's position in, 114

  obstruction after thyroidectomy, 748

  after use of Avertin, 96

  rate in acidosis, 25

  in alkalosis, 25

  tract infection as contraindication to operation, 107, 364

  in children, 192

  postoperative complications of, 358

Rest in cardiac disease, 238, 240

  in gastric hemorrhage, 628

  in hyperthyroidism, 729, 741

  in preparation for chest surgery, 571, 594

  in shock, 144, 145

  in thrombophlebitis, 398

  postoperative, 118, 128

  preoperative, 108

Restlessness as symptom of postoperative hemorrhage, 495

Retention of base, 26, 28

  of chloride, 26, 33

  of fluid, 31, 34

  of salt, 27, 31, 34

  of urinary constituents, 23

  sutures, 464

Rh blood types, 169 (*see also* Blood, Rh Type)

Rheumatic heart disease, 236, 239

Rib, fracture of, 564

  resection of, in empyema, 557, 558

Riboflavin, 210, 546

Ringer's solution, 36, 38

Rochelle salt, 663, 682

Roentgenography (*see* X-ray)

Rose bengal test of liver function, 697, 702

Rouleaux in blood cross-matching, 167

Rubber sheet as protective skin dressing, 659

# Rubber—Cont'd

sponge in fixation of intercostal catheter, 555, 559

tissue as drainage material, 492

tube as drainage material, 492

# S

Saline wheal test, 762

Saliva, digestion by, 50

Salivary fistula, 513

Salt (*see* Sodium Chloride)

Salyrgan, 241, 741

Saprophytic organisms, gas-producing, 504

Scarlet fever, glomerulonephritis after, 254

  red ointment in wounds, 345, 488

Schlesinger's solution, 118

Scopolamine in preoperative medication, 93

Scurvy, diagnosis of, 218, 226

  vitamin C in, 211

Season, relation to venous thrombosis, 383

Seconal, 85, 93, 96, 232

Secondary anemia, 214

  closure of wound, 467

  operation for choledocholithiasis, 719

  for hemorrhage, 352, 495, 718

  for wound dehiscence, 501

shock, 134, 145

Sedation in aged patient, 200

  in angina pectoris, 248

  in children, 119

  in congestive heart failure, 240, 242

  in diffuse peritonitis, 447

  in gastric hemorrhage, 628

  in hypertension, 251

  in hyperthyroidism, 729, 743

  in infants, 196

  in intestinal obstruction, 420

  in postoperative nausea, 320

  in tachycardia, 233

  in tetanus, 511

  postoperative, 118

  preoperative, 108

Sedimentation rate in gynecology, 781

Sensitivity, serum, 58, 509

  to catgut, 500

Sepsis, anemia in, 214

  in empyema, 551

  in infected gangrene, 769

  oral, 107, 202

Septicemia, 353, 652

  treatment of, 354

Serial bromsulfalein test of liver function, 697

Serine, 59

Serologic blood groups, 165

Serum, 63

*accumulation of, in wound*, 196

  agglutinins, 165

  albumin, 62

    Army and Navy Package of, 151

    concentrated, 151

  globulin, 62

  immune, in septicemia, 356

  protein (*see* Plasma protein)

  sensitivity, 59, 509

    treatment of, 510

  transfusion of, 149

Shock, 132

  after blood transfusion, 182

  albuminuria in, 256

  as cause of protein loss, 64

  as contraindication to Avertin, 97

    to operation, 110

  associated with hemorrhage, 134, 137, 139, 142, 161, 350

  blood pressure in, 142, 155

    volume in, 139, 142, 149

  contrast to cardiac failure, 133

  crush syndrome in, 140

  death cycle in, 138

  diagnosis of, 141, 155

  factors predisposing to, 67, 143

  hematocrit determinations in, 142

  hemoconcentration in, 138, 139, 142, 149

  hypoglycemic, 265, 271

  impending, 144

  in acute gastric dilatation, 451, 619

  in burns, 523, 525, 532, 535

    treatment of, 525, 532

  in diabetic patient, 270

  in gangrene of extremity, 770

  in gas gangrene, 504

  in hypertensive patient, 142, 252

  in intestinal obstruction, 421

  in peptic ulcer hemorrhage, 629

  in perforated peptic ulcer, 630

  in pulmonary embolism, 402

  in spinal anesthesia, 100

  in thoracic injury, 564

  increased susceptibility in protein deficiency, 66

  insulin, 265, 271

  irreversible, 137, 140

  mechanism of, 138

  morphine poisoning in, 95, 532

  oliguria in, 140

  pathogenesis of, 133

  physiologic changes in, 137

## Shock—Cont'd

  plasma loss in, 135, 136, 137

  postoperative, 139, 349

    in aged patient, 199

    in gastric surgery, 615, 617

    in hypertensive patients, 252

    in infants, 195

    in thoracic surgery, 577

    in ulcerative colitis, 658

  premonitory signs of, 144

  primary, 133, 155

    stimulant drugs in, 144

  prophylaxis of, 143, 155

  relation of emotional factors to, 134

    to kidney damage, 137, 140, 141, 523

  retardation of blood flow in, 804

  secondary, 134, 155

  studies on, during World War II, 137

  symptomatology of, 142

  theory of, hematogenic, 136, 137

    neurogenic, 134, 137

    toxigenic, 135, 137

  treatment of, 144, 156, 805

    with adrenal cortical extract, 154, 156

    with blood substitutes, 152

      transfusion, 68, 138, 146, 156, 161

    with gelatin, 152, 156

    with gum acacia, 152, 156

    with local heat, 145, 156

    with normal salt solution, 154, 156

    with oxygen, 155, 804

    with pectin, 153, 156

    with plasma transfusion, 162

    with serum albumin transfusion, 151

    with stimulant drugs, 146

    urinary output in, 68, 140

    vicious circle in, 137

Sickle-cell anemia, 217

Sickling test, 217

Sigmoid colon, carcinoma of, 680

Sigmoidoscopy, 680

Sign, Branham, 774

  Chvostek, 752

  Homans, 384

  Trousseau, 752

Silk as burn dressing, 530

Silver nitrate as bladder instillation, 333

  as hemostatic agent, 490

  as tanning agent, 526

  wire sutures, in postoperative wound dehiscence, 501

Singultus (*see* Hiccough)



Sinus arrhythmia, 233  
 definition of, 511  
 Siphon drainage of pleural cavity, 556  
   of stomach, 324,  
 Sippy diet, 629  
 Sitz bath, 682, 687, 688  
 Skim milk powder in high protein diet, 72, 74  
   in severe malnutrition, 545, 560, 616, 657, 703, 730  
 Skin, atrophic changes in, 761  
   bacterial flora of, 477  
   care of, 344  
   in duodenal fistula, 621  
   in enterostomy, 645  
   in ileostomy, 659  
   color of, in gas gangrene, 504  
   in hemorrhage, 351  
   in peripheral vascular disease, 759, 760  
   in shock, 142  
   decubitus ulcer of, 343  
   disinfection of, 476  
   effects of scrubbing upon, 476  
   examination of, in occlusive arterial disease, 759  
   grafting, in burns, 525, 541, 542  
   in open wounds, 476  
   in pruritus ani, 688  
   maceration of, by wet dressings, 471, 473, 757  
   rash in bromide intoxication, 83  
   in penicillin therapy, 300  
   in streptomycin therapy, 314  
   in sulfonamide intoxication, 279, 285, 289, 291  
   temperature of, in peripheral vascular disease, 759  
   traction, after open amputation, 772  
 Slough after alcohol injection, 688  
   burn, 522, 525, 541  
   removal of, 541, 543  
 Small bowel (*see* Intestine, small)  
 Smith test for prothrombin deficiency, 223  
 Soap as cleansing agent in wounds, 476  
 Sodium acid phosphate for acidification of urine, 338, 341  
   amylal, 511  
   benzoate in test of liver function, 699  
   bicarbonate in gastric lavage, 321, 607, 608  
   in sulfonamide therapy, 250, 282, 286, 288  
   in transfusion reaction, 184  
   of blood plasma, 25, 26, 28

## Sodium—Cont'd

chloride (*see also* Normal salt solution, Fluid replacement therapy):  
   deficiency of, 27  
   depletion of, 32  
   excessive administration of, 27, 31  
   excretion of, 27, 31  
   intake of, 26, 27, 30, 78  
   loss of, from enterostomy, 645, 660  
   in burns, 523  
   in gastric suction drainage, 30, 324  
   in intestinal obstruction, 417, 418  
   postoperative intolerance to, 32  
   replacement of, in infant, 22, 193, 194  
   restriction of, in congestive heart failure, 240, 242  
   in nephritis, 259  
   retention of, 27, 34  
   solution, hypertonic, in intestinal distention, 327, 441  
   in thromboangiitis obliterans, 766  
 citrate as anticoagulant, 176  
 evipal, 100  
 iodide, 739  
   as expectorant, 319  
 ion, 23, 26, 28, 31  
 lactate, use of, contraindicated in alkalosis, 34  
   in acidosis, 33  
   in alkalization of urine, 33  
   in crush syndrome, 141, 156  
   in sulfonamide therapy, 280, 291, 339  
   in transfusion reaction, 184  
 pentothal, 99, 100, 101  
   in diabetic patient, 270  
   in tetanus, 511  
 perborate as mouthwash, 202  
 phenobarbital, 119, 120  
   retention of, 26, 28, 33  
 sulfadiazine, 290, 675  
 tetrathionate, in peripheral vascular disease, 767  
 Spasm in parathyroid tetany, 752  
   in tetanus, 508  
   of sphincter of Oddi, 715  
   vascular 400, 763, 767  
 Specific gravity of urine, 23, 26, 27, 28, 29  
   in renal disease, 255, 257  
 Spherocytosis, 705  
 Sphincter, anal, atonic, in pelvic abscess, 651

- Sphincter, anal—Cont'd  
 division of, 687  
 incontinence of, 686, 687  
 of Oddi, edema of, 719  
 impaired function of, 716  
 injury to, 719  
 relaxation of, 715  
 response of, to atropine, 715  
 to food, 713  
 spasm of, 714
- Spinal anesthesia (*see* Anesthesia, spinal)
- Spirillae in oral sepsis, 202
- Splanchnic block in treatment of anuria, 261
- Splenectomy for hemolytic jaundice, 705
- Splint for amputation stump, 772
- Spores, 503, 507
- Sprain, postoperative, of neck, 112
- Spur in colostomy, 672, 673  
 in fistula, 514
- Sputum, diagnostic study of, 574
- Staphylococcus, effect of penicillin on, 297, 303, 481  
 of streptomycin on, 311  
 of sulfonamides on, 287, 288, 290, 480  
 of tyrothricin on, 481, 484  
 in burn infection, 538, 539  
 in flora of skin, 477  
 in peritonitis, 444  
 in postoperative parotitis, 410  
 in septicemia, 354  
 in subphrenic space infection, 408  
 in urinary tract infection, 338  
 in wound infection, 465, 475, 486, 496
- Starvation, acidosis in, 28, 57, 125  
 contributory to postoperative shock, 143  
 in gastric disease, 605  
 metabolism in, 78  
 postoperative, 125  
 protein requirement in, 61, 79
- Steam Inhalation, 318, 319  
 before postural drainage, 576  
 following thoracic surgery, 578
- Sterility in dressing of wounds, 459
- Stilbestrol suppository, 783
- Stoma, gastrojejunal, 624  
 obstruction of, 619, 643
- Stomach, 600 (*see also* Gastric)  
 acute dilatation of, 451, 618  
 after vagus nerve resection, 634, 636  
 hiccup in, 342, 451  
 in diffuse peritonitis, 451  
 in paralytic intestinal obstruction, 451
- Stomach, acute dilatation of—Cont'd  
 paroxysmal tachycardia in, 234  
 pathogenesis of, 452  
 postoperative, 618, 634  
 treatment of, 453  
 atony of, after vagus nerve resection, 634, 636  
 in acute dilatation, 452, 618  
 in pyloric obstruction, 610  
 postoperative, 618  
 carcinoma of, gastric analysis in, 604  
 preoperative care in, 607  
 results of treatment in, 600, 617  
 symptoms in, 607  
 contents, analysis of, 603  
 discomfort in, after gastric resection, 624  
 distention of, during intestinal intubation, 434  
 gastrointestinal series, 602  
 lavage of (*see* Gastric lavage)  
 pyloric obstruction in, 608  
 resection of, 600  
 anemia after, 626  
 dumping syndrome after, 624  
 mortality rate, 601  
 total, diet after, 616  
 mortality rate of, 617  
 postoperative care in, 615  
 preoperative care in, 608  
 types of operation, 624  
 response of, to histamine, 603  
 secretions of, 603  
 suction drainage of, 324 (*see also* Suction drainage)  
 surgery of, early ambulation after, 610  
 for bleeding peptic ulcer, 627, 629  
 for perforated peptic ulcer, 631  
 jejunostomy with, 614  
 marginal ulcer following, 626  
 postoperative care in, 610, 615  
 complications in, 617  
 diet in, 610, 612, 625  
 leakage following, 619  
 preoperative care in, 604, 606  
 lavage in, 607, 608  
 study in, 602  
 ulcer of, acute inflammatory, 605  
 complications of, 627  
 gastric analysis in, 604  
 hemorrhage from, 627  
 perforation of, 630  
 treatment with aluminum gel, 605  
 with protein hydrolysate, 606  
 vagus nerve resection for, 633

- Stool, examination of, in jaundice, 695, 704
- Strangulation in intestinal obstruction, 418, 420, 423, 426, 436
- Strap fixation of dressings, 470
- Streptogenin, 70
- Streptococcus*, anaerobic, 281
- Streptococcus fecalis*, 287, 294, 340
- Streptococcus* in burn infections, 538, 539
- in flora of skin, 477
- in oral sepsis, 202
- in peritonitis, 444
- in pharyngitis, 318
- in septicemia, 354
- in subphrenic space infection, 408
- in wound infection, 465, 475, 486, 496
- microaerophilic, 486
- Streptomyces griseus*, 306
- Streptomycin, 276, 306
- administration of, 307
- effect on commoner bacteria, 310
- fastness, 312
- in bacteremia, 313
- in burns, 539, 544
- in colonic surgery, 296, 664
- in gas gangrene, 506
- in intestinal antisepsis, 296, 664
- in peritonitis, 313, 448
- in septicemia, 358
- in thoracic surgery, 579
- in ulcerative colitis, 657
- in urinary tract infection, 313, 340
- in wound infection, 675
- indications for use of, 309
- local use of, 482
- sensitization to, 314
- standard of activity of, 307
- therapy, principles of, 311
- toxic effects of, 314
- Stricture of common bile duct, 719
- Stridor in vocal cord paralysis, 749
- String sign, 642
- Strophanthin G, 246
- Stupes, turpentine, 326, 441, 450
- Subphrenic space infection, 406, 649
- after peptic ulcer perforation, 407
- diagnosis of, 409
- hiccup in, 342
- in appendical peritonitis, 445, 651
- postoperative, 624, 632
- relation to Fowler position, 115
- treatment of, 410, 493
- Succinylsulfathiazole (see Sulfasuxidine)
- Succus entericus, 51
- Sucking wound of chest, 564
- Sucrose solution, 34
- Suction apparatus, use of in anesthetized patient, 113
- drainage, gastric (see also Gastric suction drainage):
- after vagus nerve resection, 635
- by Abbott-Rawson tube, 613
- in acute dilatation of stomach, 453, 618
- in appendical abscess, 650
- in duodenal fistula, 621
- in gastric surgery, 610, 616, 618, 635
- in gynecologic surgery, 785
- in mechanical intestinal obstruction, 426, 642
- in paralytic intestinal obstruction, 441
- in peritonitis, 447
- in postoperative wound dehiscence, 502
- in preoperative preparation, 194
- in biliary tract disease, 325
- in congenital hypertrophic pyloric stenosis, 194
- in gastric disease, 325, 607, 608
- in intestinal obstruction, 436
- surgery, 427
- in prophylaxis of intestinal obstruction, 324, 424, 426
- of postoperative distention, 429
- loss of electrolytes during, 425, 430
- postoperative, 631, 642, 658
- in gastric surgery, 610, 613, 616
- in vagus nerve resection, 635
- replacement of electrolytes during, 30, 425
- in empyema, 555
- in ileostomy, 658
- in thoracic surgery, 562, 576, 580, 581, 582
- Sugar, blood, control of, in diabetes, 263, 271
- effects of insulin on, 53
- physiologic regulation of, 52
- Sulfacetimide, 296
- use of, in urinary tract infection, 296, 339
- Sulfadiazine, 290
- absorption of, 290
- acetylation of, 290
- administration of, 290
- in bronchopneumonia, 373
- in burns, 539, 540

**Sulfadiazine—Cont'd**

- in gastric surgery, 608
- in oral sepsis, 203
- in peritonitis, 448
- in prophylaxis of infection, 290
- in pulmonary atelectasis, 372
- in septicemia, 356
- in thoracic surgery, 579
- in urinary retention, 335
- tract infection, 338
- in wound infection, 486
- local use of, 283
- toxic effects of, 291

**Sulfaguanidine as intestinal anti-septic, 293****Sulfamerazine, 292****Sulfamylon in treatment of infected wounds, 483****Sulfanilamide, 281**

- administration of, 281
- in septicemia, 356
- in urinary tract infection, 281
- in World War II, 283
- local use of, 281, 283, 479
- in burns, 539
- in peritoneal cavity, 284, 631, 637
- in thoracic cavity, 284
- precautions during use of, 285
- solution as wet dressing, 471
- as wound irrigation, 677
- toxic effects of, 285

**Sulfapyridine, 287****Sulfastixidine as intestinal anti-septic, 294, 663**

- effects on feces, 294
- in colon surgery, 294, 663, 667
- in gynecologic surgery, 783
- in ulcerative colitis, 656

**Sulfathalidine as intestinal anti-septic, 295, 669**

- in colon surgery, 295, 663, 667
- in gynecologic surgery, 783
- in ulcerative colitis, 656

**Sulfathiazole, 287**

- absorption of, 287
- acetylation of, 287
- administration of, 288
- effects of, on urinary tract, 289
- in septicemia, 356
- local use of, 289, 480
- in burns, 540
- sensitization to, 289
- toxic effects of, 289

**Sulfocyanates in hypertension, 251****Sulfonamide drugs, 276**

- absorption of, 278
- acetylation of, 278
- administration of, 278, 279

**Sulfonamide drugs—Cont'd**

- as cause of anuria, 281, 286, 289, 291
- combinations of, 292, 339, 357, 373
- concentration of, in blood, 279
- excretion of, 278
- in aspiration pneumonia, 374
- in bronchitis, 319
- in carbuncle, 347
- in cellulitis, 756
- in empyema, 559
- in gas gangrene, 506
- in oral sepsis, 202
- inhibitors of, 277, 283
- limitations of, 277
- local use of, 283, 479
- in burns, 285
- in peritoneal cavity, 285
- mode of action of, 277
- prophylactic use of, 283
- sensitivity to, 281, 289
- therapeutic effects of, 278
- toxic effects of, 279, 285, 289, 291
- treatment for, 33, 280, 286
- upon urinary tract, 280, 281, 286, 289, 291
- use of alkalis with, 280, 286, 288, 290

**Sulfuric acid, 25****Sump drain in appendical peritonitis, 653****in duodenal fistula, 621****Surface area, estimation of, as guide to therapy in burns, 534****Surgeon, responsibility of, to patient, 19, 416****Surgery, emergency, preparation for, 110****indications for, in chest wound, 564****legal authorization for 103****relation to physiology 102****Surgical mortality in bleeding peptic ulcer, 627, 629****in pneumonectomy, 581****operation, protein deficiency following, 64****relation to pulmonary atelectasis, 365****to urinary retention, 328****risk in aged subjects, 197****in cardiac disease, 230****in children, 192****in diabetes, 262****in gastric disease, 601****in hypertension, 250****in nephritis, 254, 255****in perforating peptic ulcer, 630**

- Surgical risk—Cont'd  
   in pregnancy, 226  
   in pulmonary tuberculosis, 592  
   in thoracic disease, 572, 583  
   in ulcerative colitis, 657  
 Suture materials, relation to early ambulation, 131, 786  
   to healing, 131  
   to wound dehiscence, 500  
 Sutures, removal of, 463  
   after thyroidectomy, 747  
 Sweat, fluid loss in, 22  
 Symbiosis, 276  
 Sympathectomy (*see* Ganglionectomy, sympathetic)  
   periarterial, 768  
 Sympathetic ganglion block in arteriovenous fistula, 777  
   in occlusive arterial disease, 763, 767  
   lumbar, in thrombophlebitis, 399  
     technique of, 399  
 Syncope, 133, 155, 233, 402  
 Synthesis of amino acids, 59, 693  
   of ammonia, 26  
   of fat, 55, 693  
   of glucose, 51, 53, 126, 693  
   of heparin, 694  
   of plasma proteins, 62, 694  
   of protein, 61  
   of prothrombin, 219, 694  
   of thyroid hormone, 724, 725, 726, 732  
   of urea, 61, 693  
 Syphilis in surgical patient, 104, 105, 203  
 Syphilitic heart disease, 246  
   as contraindication to spinal anesthesia, 246  
 Systolic pressure in shock, 142, 143

## T

- Tachycardia, during blood transfusion, 179, 182  
   in hyperthyroidism, 727, 729, 739  
   in thyroid crisis, 743  
   paroxysmal, 234  
 Tannic acid in treatment of burns, 522, 525  
   liver damage caused by, 522, 526  
 Tanning agents in treatment of burns, 526  
 Teeth, preoperative care of, 107, 203, 572  
 Tendon sheaths, infection of, 756, 757

- Temperature in shock, 142  
   of fluids for infusion, 43  
   of skin after sympathectic ganglion block, 763  
     elevation of, by fever therapy, 766  
   in occlusive arterial disease, 759, 760  
   in refrigeration anesthesia, 770  
 Tension, pneumothorax, treatment of, 567  
 Tent, oxygen, 806  
 Test for bleeding tendency, 220  
   for hemophilia, 219  
   for scurvy, 218  
   for sickle-cell anemia, 217  
   for thrombocytopenic purpura, 225  
     heparin tolerance, 382  
     histamine flare, 762  
     in jaundice, 695  
     Matas-Moszkowicz, 776  
     of capillary resistance, 218  
     of kidney function, 257  
     of liver function, 697  
     saline wheal, 762  
 Testosterone, use of, in endometriosis, 783  
   in uterine bleeding, 783  
 Tetanus, 507  
   antitoxin, 505, 508, 509, 769  
   in burns, 532, 538, 539  
   in crushing injury, 141  
   intravenous administration of, 510  
   subcutaneous administration of, 508, 509  
     diagnosis of, 508  
     prophylaxis of, 508  
     pulmonary atelectasis in, 510  
   toxoid, 505, 508  
   treatment of, 509  
   use of Avertin in, 97  
   wounds likely to be associated with, 507  
 Tetany caused by vomiting, 190  
   parathyroid, 757  
     calcium in, 752  
     phosphorus in, 752  
     symptoms of, 752  
     treatment of, 752  
 Tetraethylammonium bromide, 400  
   chloride, 767  
 Tetraiodophenolphthalein for gall bladder visualization, 803  
   test of liver function, 698  
   use of, contraindicated in biliary colic, 708  
 Theobromine, 241  
 Theophylline, 241

- Thiamine hydrochloride (*see* Vitamin B<sub>1</sub>)
- Thiouracil as substitute for thyroidectomy, 734  
 dosage of, 735  
 effects of, 732  
 hypothyroidism caused by, 732, 735  
 in hyperthyroidism, 731  
 in prevention of thyroid crisis, 742, 744, 747  
 indications for use of, 734, 741  
 toxic effects of, 733, 735  
 use of, with iodine, 736, 737
- Thiourea, 726, 731
- Thirst in dehydration, 22, 27  
 in postoperative hemorrhage, 351
- Thoracentesis, diagnostic, in intrathoracic disease, 574  
 following thoracic surgery, 576, 580, 582, 616  
 in empyema, 553  
 in hemothorax, 568, 570  
 in tension pneumothorax, 567  
 in thoracic injury, 565
- Thoracic surgery (*see* Chest, surgery of)
- Thoracoplasty, 592  
 dressing, 595  
 following pneumonectomy, 579  
 pulmonary resection for tuberculosis, 597  
 postoperative care in, 594  
 preoperative care in, 593
- Thoracotomy in hemothorax, 568, 570  
 indications for, in chest wound, 564
- Threonine, 59
- Thrombin, topical, as hemostatic agent, 490
- Thromboangitis obliterans, 759, 764  
 drugs used in treatment of, 766  
 fever therapy in, 766  
 postural exercises in, 766  
 sympathetic ganglionectomy in, 767
- Thrombocytopenic purpura, 224  
 treatment of hemorrhage in, 352
- Thrombophlebitis, 377  
 diagnosis of, 384  
 in gynecologic surgery, 790  
 pathogenesis of, 380  
 puerperal septic, 355  
 relation of protein deficiency to, 67  
 skin changes in, 759  
 treatment of, 397
- Thromboplastin as hemostatic agent, 490  
 in blood-clotting mechanism, 163
- Thrombosis, coronary (*see* Coronary thrombosis)  
 venous, anticoagulant treatment of, 387  
 combined treatment of, 395  
 diagnosis of, 383  
 factors contributory to, 381, 383  
 in appendical peritonitis, 651  
 in gynecologic surgery, 790  
 in nonsurgical patients, 377  
 incidence of, 377  
 pathogenesis of, 378  
 postoperative, 377  
 preoperative, 791  
 prophylaxis of, 385  
 relation of Fowler position to, 115, 381  
 of heparin tolerance test to, 382  
 of pulmonary embolism to, 401  
 surgical treatment of, 392
- Thymol turbidity test, 701
- Thymus gland, 192
- Thyrocardiac disease, 229, 236, 739  
 auricular fibrillation in, 741  
 heart failure in, 742  
 thyroidectomy in, 741  
 use of thiouracil in, 734
- Thyroid, carcinoma of, use of radioactive iodine in, 739  
 crisis, 725, 727, 735, 742, 747  
 cardiac failure in, 744  
 mortality rate of, 743  
 prevention of, 742, 743  
 signs of, 742, 748  
 treatment of, 743, 748  
 disease, latent, 233  
 gland, effects of iodine on, 738  
 of thiouracil on, 732, 735  
 hyperplasia of, 724, 726, 732  
 involution of, 736, 737  
 relation to pituitary gland, 725, 726, 732  
 hormone, excess secretion of, 724, 725  
 relation to pituitary thyrotropic hormone, 725, 726, 732
- Thyroidectomy, 725  
 anesthesia in, 750  
 contraindications to, 745  
 difficulty of, after thiouracil therapy, 735, 737  
 in thyrocardiac disease, 741  
 injury to inferior laryngeal nerve during, 748

- Thyroidectomy, injury—Cont'd  
   to parathyroids during, 731  
   postoperative care in, 745  
   complications of, 747  
   when to perform, 744
- Thyrototoxicosis (*see also* Hyperthyroidism):  
   etiology of, 724
- Thyrotropic hormone, 724, 725, 732
- Thyroxine, 725 (*see also* Thyroid hormone)
- Tidal drainage apparatus for urinary bladder, 336
- Tinnitus caused by streptomycin, 314
- Tissues, biochemical balance of, 21
- Tobacco in occlusive arterial disease, 765  
   relation to venous thrombosis, 383, 386, 389
- Toluidine blue in treatment of purpura, 225
- Tonsillitis, 107, 192
- Tourniquet, 769  
   test in parathyroid tetany, 752  
   in purpura, 225  
   in scurvy, 218
- Toxemia in diffuse peritonitis, 444  
   in gas bacillus infection, 504, 505  
   in intestinal obstruction, 418, 419, 421
- Toxic effects of digitalis, 244  
   of penicillin, 300, 301  
   of streptomycin, 314  
   of sulfonamide drugs, 279  
   theory of liver death, 720  
   thyroid disease (*see* Hyperthyroidism)
- Toxin as cause of shock, 135
- Trachea, collapse of, after thyroidectomy, 749  
   displacement of, in thyroid disease, 729, 749
- Tracheitis after thyroidectomy, 747, 751  
   caused by burns, 537  
   preoperative, 107
- Tracheobronchial suction catheter, 369  
   following thoracic surgery, 578, 597  
   in treatment of wet lung, 566
- Tracheobronchitis, postoperative, 318, 358
- Tracheotomy in laryngeal edema, 537  
   in paralysis of inferior laryngeal nerves, 749  
   in tracheal collapse, 750
- Traction, skin, 772
- Transfusion apparatus, Baxter, 815  
   Cutter, 824  
   Upjohn, 831
- Transfusion, blood, 159  
   administration of, 178  
   amount required, 148  
   banks (*see* Blood banks)  
   collection of, 175, 180  
   compatibility, 165, 168  
   contraindications to, 164  
   direct, 174  
   during heparin treatment, 389  
   during operation, 19, 111, 576, 590  
   in aged patient, 199  
   in anemia, 162, 216  
   in anticoagulant overdosage, 392  
   in arteriovenous fistula repair, 776  
   in biliary tract disease, 702  
   in burns, 68, 525, 535, 545, 546  
   in cardiac disease, 164  
   in chronic protein deficiency, 69  
   in colon surgery, 662, 668, 675  
   in congenital hypertrophic pyloric stenosis, 194  
   in decubitus ulcer, 345  
   in delayed convalescence, 160  
   wound healing, 499  
   in duodenal fistula, 623  
   in emergency surgery, 110  
   in empyema, 560  
   in enterostomy patient, 645  
   in gas bacillus infection, 507  
   in gastric surgery, 604, 606, 607, 608, 609, 610, 616, 617  
   in gastroenteric stomal block, 619  
   in gynecologic surgery, 782, 784  
   in hemolytic jaundice, 216, 705  
   in hemophilia, 219  
   in hemorrhage, 159, 161  
   in hemorrhagic states, 163, 707  
   in hemothorax, 569  
   in hyperthyroidism, 731  
   in hypoproteinemia, 63, 162  
   in infants, 193, 195  
   in infected gangrene, 769  
   in intestinal obstruction, 436, 437  
   in liver damage, 703  
   in malnutrition, 162  
   in paralytic intestinal obstruction, 441  
   in peptic ulcer hemorrhage, 628, 630  
   perforation, 630  
   in peritonitis, 446, 449

Transfusion, blood—Cont'd  
 in postoperative hemorrhage, 352, 496  
 in preoperative care, 162  
 in prophylaxis of shock, 110, 143  
 in prothrombin deficiency, 707, 710, 717  
 in purpura, 225  
 in septicemia, 356  
 in shock, 68, 138, 146, 156, 161  
 in sickle-cell anemia, 217  
 in skin-grafting of burns, 512  
 in surgery of pulmonary tuberculosis, 594, 596  
 in thoracic surgery, 563, 564, 578, 590  
 in ulcerative colitis, 657, 658  
 in wound dehiscence, 502  
 infection, 476  
 incompatible, 165, 170, 182  
 indications for, 159  
 indirect, 175  
 intramedullary, 44, 181  
 intraperitoneal, 43  
 postoperative, 632, 710, 717  
 preoperative, 106, 107, 371, 590  
 rate of administration of, 179  
 reactions to, 140, 170, 179, 181, 187, 236  
 allergic, 185  
 hemolytic, 181  
 pyrogenic, 184  
 Rh incompatibility, 170  
 Rh type, 169  
 transmission of disease by, 181  
 universal donor, 166  
 with heparinization of donor, 174  
 plasma, in burns, 68, 525, 532, 533, 536, 545  
 in hemolytic jaundice, 705  
 in hypoproteinemia, 63  
 in shock, 139, 147, 156  
 red blood cell suspension, 186  
 serum, 149  
 albumin, 152  
 Trauma, protein deficiency following, 64  
 Trendelenburg operation, 405  
 position, 385, 577, 615  
*Treponema pallidum*, effect of penicillin on, 297  
 Triple dye as tanning agent, 526  
 sulfonamides, 292  
 Trousseau's sign, 752  
 Trypsin in digestion of protein, 60  
 Tryptophan, 59, 70  
 Tuberculosis [pulmonary (*see* Lung, tuberculosis of)]

Tularemia, 313  
 Turpentine stipes, 326, 441, 450  
 Typhoid vaccine for fever therapy, 766  
 Typing, blood, 166  
 Rh, 171, 172  
 Tyrosine, 59  
 Tyrothricin, 276  
 in treatment of infected wounds, 483, 768

## U

Ulcer, decubitus (*see* Decubitus ulcer)  
 leg, healing of, 67  
 peptic (*see also* Stomach, ulcer of, Duodenum, ulcer of).  
 complications of, 627  
 hemorrhage from, 627  
 perforation of, 630  
 after vagus resection, 634  
 mortality rate in, 630  
 vagus resection for, 633  
 stomal, 626, 634  
 Ultraviolet radiation, 345  
 Umbilical hernia repair, 365  
 Undulant fever, 104  
 United States Army, blood transfusion service in, 187  
 Universal blood donor, 166  
 Urea, blood, 258, 260  
 clearance test, 258  
 formation in liver, 61, 693  
 in treatment of sloughing wound, 488  
 in urine, 62  
 nitrogen, serum, 799  
 subnormal formation of, 693  
 Urecholine, 636  
 Uremia, 182, 260  
 as cause of hiccough, 342  
 Ureter, identification of, 792  
 operative injury to, 675, 792, 793  
 preoperative catheterization of, 792  
 Ureters, catheterization of, in sulfonamide block, 281  
 Urethane in treatment of wound infection, 487  
 Uric acid, metabolism of, 693  
 serum, 800  
 Urinalysis, 256  
 false positive sugar test in, 84  
 in cystitis, 338  
 in dehydration, 23, 28  
 in diabetes, 264, 271  
 in diabetic coma, 268  
 in diagnosis of postoperative febrile state, 337



## Urinalysis—Cont'd

in jaundice, 695, 704

preoperative, 104, 647

## Urinary bladder, automatic tidal drainage apparatus,

336

catheterization of, 333, 676

preoperative, 784

constant drainage of, 335, 676

retention catheter in, 335

## casts, 256

changes in crush syndrome, 140

concentration test, 257

constituents, retention of, 23, 29

incontinence, 676

output, 22, 23, 27, 29, 30

in burns, 68

in crushing injury, 140, 141

in intestinal obstruction, 417

in nephritis, 254, 255

in postoperative vomiting, 123

in shock, 68, 136

in transfusion reaction, 182

in uremia, 260

minimum, 78

optimum, 324

postoperative, 123, 330

overflow incontinence, 330

retention, 328

after resection of rectum, 676

diagnosis of, 329

in aged patient, 201

in gynecologic patient, 787

postoperative, 328

prophylaxis of, 328

psychic factors in, 332

treatment of, 331

sugar, control of, in diabetes, 263

quantitative determination of,

272

tract infection, factors predis-

posing to, 337

hematuria in, 257

in gynecologic patient, 782

symptoms of, 337

treatment of, 297, 338

with penicillin, 340

with streptomycin, 313

with sulfacetamide, 296

with sulfadiazine, 290

with sulfathiazole, 287

## Urine, acidification of, 341

alkalinization of, 280

in crush injury, 33, 141

in sulfonamide therapy, 33, 280,

286, 288, 291, 339

in transfusion reaction, 33, 183,

184

bicarbonate in, 26, 29

blood in, 256

## Urine—Cont'd

collection of, in infants, 191

in vesicovaginal fistula, 791

concentrated, 23, 26

dilute, 26

excretion of, 26, 123, 256

in glomerulonephritis, 255, 256

ketones in, 58, 123, 266

loss of carbohydrate in, 38

nitrogen excretion in, 61, 65

output of, as guide to therapy in

burns, 535, 537

pH of, 341

postoperative leakage of, 676

secretion of, 329

protein content of, 256, 259

residual, 330, 333, 335, 676

retention of, in appendical peri-

tonitis, 651

in gynecologic surgery, 787

postoperative, 676

specific gravity of, 23, 26, 27,

28, 29

in nephritis, 255, 257

suppression of, in sulfonamide

toxicity, 281, 286, 289

291

Urobilinogen, formation of, 694

in urine, 695, 704

Urologic complications, postopera-

tive, 675

disease simulating surgical con-

dition, 110

Urticaria caused by penicillin, 300

following blood transfusion, 185

Uterus, perforation of, 791

## V

Vagina, senile changes in, 783

Vaginal drainage of pelvic abscess,

652

examination in intra-abdominal

hemorrhage, 351

Vaginitis, preoperative treatment

of, 782

Vagotomy (see Vagus nerve resec-

tion)

Vagovagal reflex, 566, 577

Vagus nerve, relation to acute dila-

tation of stomach, 452

resection of, 633

disadvantages of, 634

dumping syndrome after, 626

effects of, 633

for peptic ulcer, 634

indications for, 634

insulin test after, 636

transabdominal, 635

transthoracic, 635

use of Urecholine after, 636

- Vagus nerve, resection—Cont'd  
with complementary gastro-  
enterostomy, 634
- Valine, 59
- Val-salva experiment, 401
- Van den Bergh test, 696, 704
- Van Slyke urea clearance test, 258
- Varicose veins, relation to venous  
thrombosis, 383
- Vascular disease, occlusive, of ex-  
tremities, 758  
surgery, sympathetic ganglion-  
ectomy in, 767
- Vasoconstricting drugs in shock,  
144, 146, 155, 156  
in spinal anesthesia, 100
- Vasodilatation for increase of col-  
lateral circulation, 766,  
767
- Vasodilating drugs, use of, in angina  
pectoris, 248  
in hypertension, 251  
in occlusive arterial disease  
of extremity, 767
- Vasospasm in occlusive arterial  
disease, 763, 767  
in pulmonary embolism, 403  
in thrombophlebitis, 763, 767
- Vein, ligation of, in occlusive  
arterial disease, 767  
in septicemia, 355
- Veins, femoral, ligation of, 387  
iliac, ligation of, 394  
lower leg, as site of venous throm-  
bosis, 378
- Vena cava, ligation of, 355  
in suppurative thrombophle-  
bitis, 394  
in venous thrombosis, 394
- Venesection in congestive heart  
failure, 243
- Venipuncture in infants, 195  
technique of, 39, 177
- Venoclysis (see Infusion. Fluid  
replacement therapy)
- Venography, 761
- Venous congestion in valvular heart  
disease, 239  
pressure in shock, 133  
stasis as contributory cause of  
thrombosis, 381  
in pulmonary atelectasis, 360  
thrombosis (see Thrombosis)
- Vertigo caused by streptomycin, 314
- Vinegar as vaginal douche, 794
- Visceral function, effect of protein  
deficiency on, 67
- Viscus, perforation of, as cause of  
peritonitis, 442, 443,  
444  
caused by drains, 492
- Visitors to patient, 192
- Vital capacity, 129  
in empyema, 550  
preoperative, 572, 593
- Vitamin A, 207, 691  
B complex, 208, 211  
relation to wound healing,  
458, 499
- B<sub>1</sub> in aged patient, 200  
relation to carbohydrate me-  
tabolism, 79
- B<sub>2</sub> (see Nicotinic Acid)
- B<sub>6</sub> (see Pyridoxine)
- C, 211  
deficiency of, 80  
diagnosis of, 218, 226  
in burns, 546  
in surgical patient, 80  
plasma, 798  
relation to wound healing,  
130, 458, 499, 500, 502
- D, 211  
in hypoparathyroidism, 753  
deficiency as cause of stomal ob-  
struction, 619  
in aged patient, 199  
in gastric disease, 601  
in hyperthyroidism, 730  
in hypoproteinemia, 67  
in ulcerative colitis, 657  
preoperative correction of, 107  
states, 207
- E, 212  
in peripheral vascular disease,  
767
- G (see Riboflavin)
- K, 212  
deficiency of, in obstructive jaun-  
dice, 219  
in peptic ulcer hemorrhage, 628,  
630  
in postoperative gastric hemor-  
rhage, 618  
preoperative use of, 605, 609, 612  
relation of, to prothrombin, 705,  
707  
therapy, 706, 710  
after total gastrectomy, 617  
in bleeding peptic ulcer, 630  
in burns, 546  
in carcinoma of colon, 662, 668  
in children, 194  
in decubitus ulcer, 345  
in diabetic patient, 263  
in empyema, 560  
in enterostomy patient, 645  
in gastric surgery, 605, 609, 612,  
613  
in jejunostomy feeding, 615  
in liver damage, 703  
in malnutrition, 206

- Vitamin therapy—Cont'd  
 in occlusive arterial disease, 765  
 in peritonitis, 449  
 in postgastrectomy anemia, 626  
 in septicemia, 356  
 in thoracic surgery, 579, 590  
 in thyroid crisis, 744  
 in ulcerative colitis, 657, 658  
 in wound infection, 476
- Vocal cord, paralysis of, 748  
 resection of, 749
- Vomiting, alkalosis after, 28  
 as cause of tetany, 190  
 caused by Demerol, 91  
 by morphine, 89  
 by sulfanilamide, 286  
 effect on acid-base balance, 25  
 fecal, 421  
 in acute gastric dilatation, 451, 619  
 in hyperthyroidism, 727, 731, 743, 748  
 in intestinal obstruction, 417, 419, 641  
 in peritonitis, 440, 443, 444  
 in transfusion reaction, 182  
 postoperative, 320, 785  
 as cause of wound dehiscence, 500

## W

- Wangensteen apparatus for gastric suction, 324
- War Department directives on use of sulfanilamide, 283
- War injuries, gas gangrene following, 503
- Water (*see also* Dextrose, Fluid, Normal Salt Solution, etc.)  
 daily requirement of, 29  
 excess ingestion of, 26  
 intake, estimation of, 29  
 intoxication, 26  
 proportion of, in body weight, 21  
 retention of, 31, 32
- Waterseal in drainage of pleural cavity, 555, 562  
 in treatment of tension pneumothorax, 567
- Weight, change of, in hyperthyroidism, 728  
 loss, postoperative, 64
- Welch bacillus (*see Clostridium welchii*)
- Wet dressings, 470, 682  
 lung, 566
- Whiskey in aged patient, 201
- Wool clothing, spores in, 503

- World War I, studies on shock in, 135  
 on thoracic surgery in, 552
- II, studies on burns in, 519, 535  
 on crush syndrome in, 140  
 on decubitus ulcer in, 345  
 on shock in, 137  
 on traumatic wounds in, 467, 468, 481  
 surgery of colon in, 674  
 treatment of thoracic wounds in, 563, 569  
 use of plasma transfusions during, 147  
 sodium pentothal during, 101  
 sulfanilamide during, 283
- Wound, anaerobic infection of, 486  
 bacterial contamination of, 465, 475  
 care of, 455  
 in colostomy, 671  
 in duodenal fistula, 621  
 in enterostomy, 633  
 in ileostomy, 659  
 in obese patient, 204  
 clean, dressing of, 459  
 complications of, 495  
 dehiscence of, 499  
 after colostomy, 672, 675  
 after gastric surgery, 624  
 contributory factors in, 500  
 intubation in prophylaxis of, 429  
 symptoms of, 500  
 treatment of, 501  
 delayed healing of, 498  
 digestion of, around ileostomy, 659  
 drainage of, 491  
 in appendectomy, 648, 649  
 in perforated peptic ulcer, 631  
 dressing, 459, 465  
 after thyroidectomy, 746  
 fixation of, 469  
 in infants, 196  
 effect of protein deficiency on, 67  
 excision of, in treatment of tetanus, 509  
 healing of, 427, 455, 456  
 factors influencing, 130, 457, 498, 500  
 relation of suture material to, 131  
 vitamin C in, 211  
 hematoma of, 496  
 hemorrhage from, treatment of, 352, 489, 495  
 infected, care of, 469  
 closure of, 476

Wound, infected—Cont'd  
 dressing of, 469  
 gas gangrene in, 503  
 irrigation of, 475  
 principles of treatment of, 470  
 supportive therapy of, 476  
 tetanus in, 507  
 treatment with acetic acid, 487  
   with Azochloramid, 689  
   with bacitracin, 484  
   with nitrofurazone, 688  
   with penicillin, 301, 481, 483  
   with streptomycin, 482  
   with sulfonamide drugs, 281,  
     289, 290, 479  
   with tyrothricin, 483  
   with wet dressings, 470  
   with zinc peroxide, 486, 689  
 use of antiseptics in, 474  
   of local medication in, 474  
 Infection, 456  
   anaerobic, 507  
   after colonic surgery, 674  
   after gastric surgery, 624  
   after thoracoplasty, 594  
   after thyroidectomy, 751  
   postoperative, 496, 497, 632  
     prevention of, 496  
     symptoms of, 497  
     treatment of, 498  
 lag period of healing, 128  
 of chest (*see* Chest, wound of)  
 open, fine-meshed gauze dressing  
   in, 468  
 perineal, care of, 676  
   infection of, 677  
 postoperative pain in, 119  
 pressure dressing, indications for,  
   465  
   technique of application, 465,  
     528  
 puncture, tetanus associated with,  
   507  
 removal of sutures from, 463, 747  
 slough, removal of, 487  
 strength of, 455  
 sucking, 548, 552, 565  
 thoracoabdominal, 564  
 traumatic, cleaning of, 476  
   experience during World War  
     II, 467, 468  
   first-aid treatment of, 475  
   gas gangrene following, 503  
   secondary closure of, 467, 476  
 types commonly associated with  
   tetanus, 507  
 use of growth-stimulating sub-  
   stances in, 488  
 Wreden-Stone operation, 689

X  
 Xanthine drugs, 241  
 X-ray (*see also* Fluoroscopy).  
   evidence of pulmonary embolism,  
     402  
   of subphrenic space infection,  
     409  
 examination, bronchographic, 573,  
   584  
   following broncho-copv, 578  
   thoracic surgery, 580  
   for localization of lost drains,  
     494, 558  
   gastrointestinal series, 602  
   in arteriovenous fistula, 774  
   in carcinoma of colon, 661, 662  
     preoperative, 664  
   in diagnosis of empyema, 558  
   of fistula, 513  
   of gas gangrene, 505, 506  
   of intestinal obstruction, 421,  
     426  
   in hypertension, 253  
   in incomplete intestinal ob-  
     struction, 641, 643  
   in localization of lung abscess,  
     588  
   in pulmonary atelectasis, 362,  
     578  
     embolism, 402  
     tuberculosis, 592  
   in subphrenic space infection,  
     409  
   in suspected lung abscess, 375  
   in tension pneumothorax, 567  
   in thoracic injury, 564  
     surgery, 562, 572, 584  
   of chest, in thyroid disease, 729,  
     750  
   of extremity, 762  
   preoperative, 105  
     in aged patient, 198  
     in children, 105, 192  
   preparation for, 802  
   with passage of Miller-Abbott  
     tube, 431, 434  
 therapy in gas gangrene, 506  
   in postoperative parotitis, 411  
   in pruritus ani, 688

Y  
 Yeast, brewer's, 209

Z  
 Zephiran as antiseptic, 479  
   as vaginal douche, 782  
 Zinc peroxide in gas gangrene, 505,  
   507  
   in oral sepsis, 202  
   in tetanus, 509  
   in wound infection, 486, 689